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Hazardous Substances Summary and Full Development Plan

Interagency Regulatory Liaison Group, Washington, DC

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16. Abstract (Limit: 200 words) Four Federal agencies have outlined cooperative steps to curb the health and environmental threats posed by a group of toxic substances. In this report, OSHA, EPA, FDA, and CPSC describe the actions they have taken or plan to take in order to protect workers and the general public from disease and illness caused by the unsafe manufacture, handling, and use of twenty-four compounds. These compounds range from the plastic material, acrylonitrile, to radiation to toxic waste disposal. Acting under a year old cooperative agreement which created the Interagency Regulatory Liaison Group (IRLG), the member agencies are pooling their knowledge and resources to promote the development of the most efficient health protection programs with the least cost to the regulated industries.				
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INTERAGENCY REGULATORY LIAISON GROUP

HAZARDOUS SUBSTANCES

CPSC • EPA • FDA • OSHA

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INTERAGENCY REGULATORY LIAISON GROUP

HAZARDOUS SUBSTANCES SUMMARY

AND FULL DEVELOPMENT PLAN

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U.S. CONSUMER PRODUCT SAFETY COMMISSION
U.S. ENVIRONMENTAL PROTECTION AGENCY
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION
DEPARTMENT OF LABOR

The Interagency Regulatory Liaison Group (IRLG) has agreed, among other things, to take joint action to improve the quality of our agencies' regulations. We intend to:

- prevent duplicative regulatory requirements,
- avoid conflicts in standard setting, and
- share research, data, and analyses.

This document reflects one significant step towards meeting these objectives. It was prepared by the Regulatory Development Work Group, one of eight work groups of the IRLG. The document contains development plans for twenty-four hazardous materials for which two or more of our agencies intend to take regulatory action. In the process of developing these plans the Regulatory Development Work Group made a series of recommendations to the agencies, many of which have already been implemented. The four agencies agreed to:

- hold joint public meetings whenever feasible and appropriate;
- improve data sharing (efforts to do this are already underway within the Information Exchange Work Group);
- undertake joint economic impact analyses whenever feasible and appropriate;
- coordinate research planning (efforts in this area are already underway within the Research Planning Work Group);
- notify each other whenever one of the IRLG agencies begins to develop a new hazardous substance regulation;
- include in any proposed hazardous substance regulation published in the Federal Register a description of the efforts made to cooperate with other IRLG agencies and of measures taken in response to such efforts; and
- update the regulatory development plans quarterly and expand them as appropriate.

We welcome your comments and suggestions for further improving our joint cooperative effort.

Susan B. King, Chairman
Consumer Product Safety
Commission

Donald Kennedy, Commissioner
Food and Drug Administration

Sincerely yours,

Douglas M. Costle, Administrator
U. S. Environmental Protection
Agency

Eula Bingham, Assistant Secretary
of Labor, Occupational Safety and
Health Administration

FOREWORD

In August 1977, the heads of four federal regulatory agencies:

- the Consumer Product Safety Commission;
- the Environmental Protection Agency;
- the Food and Drug Administration; and
- the Occupational Safety and Health Administration

formed the Interagency Regulatory Liaison Group (IRLG) to ensure that the agencies work closely together in areas of common interest and responsibility.

One of eight groups established to promote better coordination was the Regulatory Development Work Group, which undertook to:

- identify hazardous materials that two or more IRLG agencies planned to regulate; and
- ask the writers of these regulations to jointly prepare a development plan describing
 - their statutory authority to regulate
 - the history of any regulations already in effect
 - the harm caused by the hazardous material
 - any opportunities for avoiding conflicts and duplication of effort and for joining in cooperative action.

This document contains development plans prepared for each of twenty-four hazardous materials and represents a significant step in reforming our mutual regulatory development processes. As a result of our work group's activity we have:

- improved communications among hundreds of federal officials in the four agencies;
- initiated efforts toward coordinated multi-agency regulatory action to avoid duplications;
- established forums for further cooperative action

To build on this initial effort the work group plans to:

- publish quarterly updates and expansions of these plans;
- maintain an "alert" system by which one agency will tell the others whenever it intends to begin work on a new hazardous material regulation and add such items to our quarterly update;
- describe in the preface to any new hazardous material regulation how the IRLG agencies worked together and the effect such joint effort had on the regulation.

You are invited to send your comments on any aspect of the work plans and on how we can present information of this sort in a way which is easier for you to use. You should direct comments regarding individual work plans to the prime contacts identified at the top of each summary and development plan. Direct any comments regarding the way information is presented and on other general issues to Henry Beal, Regulatory Development Work Group Chairman, Environmental Protection Agency, Room 3002, PM-223, 401 M Street, S. W., Washington, D. C. 20460, (202) 755-2265.

Henry E. Beal
Chairman
Regulatory Development
Work Group

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SUMMARY DEVELOPMENT
PLANS

Acrylonitrile (AN)
Summary

1. Background

The fact that AN is a potential human carcinogen has prompted FDA, OSHA and EPA to take new regulatory initiatives.

2. Issues

- A. The extent of exposure in the non-workplace environment.
- B. The potential risk of serious health effects.
- C. Economic impact of regulation.

3. Statutory Authority for Initiatives on AN

OSHA - Occupational Safety and Health Act
FDA - Food, Drug and Cosmetic Act
EPA - Clean Water Act; Clean Air Act; Federal Insecticide, Fungicide,
and Rodenticide Act; Toxic Substances Control Act
CPSC - Consumer Product Safety Act; Federal Hazardous Substances Act

4. Principal Actions/Schedules (Tentative)

- 9/23/77 - FDA revoked food additive regs for use of AN to fabricate beverage containers
- 1/17/78 - OSHA proposes permanent standard and issues emergency temporary standard
 - 1978 - FDA proposal to ban AN
 - 1978 - EPA RPAR action
 - 3/78 - OSHA Hearing on AN
 - 1978 - OSHA Final Standard on AN

5. Agency Technical Contacts

OSHA	- Gail Kleiner	523-9603
FDA	- Thomas C. Brown	472-5690
EPA	- Pat Hilgard	755-2110
CPSC	- Glen Simpson	492-6647
NIOSH	- Sonia Berg	443-3680

6. Recommendations

Agencies should share data in hearing records; cooperate in development of economic and environmental assessments; update status of AN work when new developments occur; have meetings; share all contractor data.

Arsenic
Summary

1. Background

Although there is a lack of consensus in the scientific community due to the lack of experimental data, arsenic has been implicated as a carcinogen, mutagen, teratogen, and neurotoxin. Numerous Federal regulatory actions have addressed or are in the process of addressing arsenic including: EPA Drinking Water Standards; EPA Water Quality Criteria and Effluent Limitations; EPA Air Pollution Control; review and possible cancellation of pesticide registration by EPA; possible regulation as a hazardous waste by EPA; OSHA workplace standard; FDA approval as a veterinary medicine and food additive; FDA food tolerances; and FDA food monitoring.

2. Major Issues

- A. A consistent approach to determining the exposure, source and route of the arsenic body burden and the disposition of arsenic is needed to facilitate compatible regulations.
- B. EPA is currently reviewing its carcinogen regulatory policy and the position developed may influence the nature and timing of the arsenic standard.
- C. Carcinogenicity, mutagenicity and teratogenicity of inorganic and organic arsenic.
- D. Need for common data base and coordinated review of regulatory actions.

3. Statutory Authorities

EPA - Safe Drinking Water Act
Federal Water Pollution Control Act
Clean Air Act as Amended
Federal Insecticide, Fungicide, and Rodenticide Act
Toxic Substances Control Act
Resource Conservation and Recovery Act
OSHA - Occupational Health and Safety Act
FDA - Food, Drug and Cosmetic Act

4. Principal Actions/Schedules (Tentative)

- A. Development of an issue paper delineating actions required by EPA (Office of Pesticides Programs) and OSHA to regulate the manufacture and use of wood preservatives containing arsenic.
- B. Develop a common data base and facilitate information exchange.
- C. Develop data and a common model on the sources and disposition of arsenic body-burden.
- D. Coordinate and conduct joint site inspections.

5. Principal Contacts

EPA - Al Campbell	8/629-5231 (FTS)
Bob Carton	755-4894
OSHA - Gerald Weinstein	523-9604
FDA - John Brown	443-3339

6. Recommendations

- A. Continue joint IRLG Regulatory Work Group coordination.
- B. Develop more detailed plan, including timetables and resource requirements to achieve actions.

Asbestos
Summary

1. Background

- A. Asbestos has been shown to cause fibrosis of the lung, cancer of the lung and lung cavity (pleural mesothelioma) and cancer of the abdomen (peritoneal mesothelioma and gastrointestinal cancer). Asbestos is found in the air, water, and in food supplies.
- B. All four agencies have promulgated regulations attempting to limit asbestos exposure.
- C. The policy that guides Federal action in this area is to curtail asbestos exposure.

2. Issues

The most critical need of all the agencies is for specific health effects decisions and/or research so the controversy with respect to the consequences of inhalation and ingestion of asbestos and asbestiform fiber can be resolved.

3. Statutory Authorities

EPA - Clean Air Act; Federal Water Pollution Control Act; Toxic Substances Control Act; Resource Conservation and Recovery Act; Federal Insecticide, Fungicide, and Rodenticide Act
CPSC - Consumer Product Safety Act, Federal Hazardous Substances Act
FDA - Food, Drug and Cosmetic Act
OSHA - Occupational Safety and Health Act

4. Proposed Actions and Schedules (Tentative)

EPA will complete a preliminary assessment of the asbestos problem in September. EPA is developing a technical assistance program for owners of buildings with asbestos ceilings. Asbestos is being considered for inclusion in the list of hazardous wastes. NIEHS oral asbestos studies in rats and hamsters will run until June 29, 1979. FDA will receive the results of a contract to develop an identification methodology in August 1978 and of a contract for a toxicological study of intravenously administered asbestos in June of 1979. CPSC has completed a study to determine the extent to which asbestos is used in consumer products and is currently evaluating the need for further regulatory action. OSHA is completing a technological feasibility and inflationary impact statement on the proposed 0.5 fibers/cc and 0.1 fibers/cc recommended by NIOSH.

5. Principal Contacts

EPA - Bob Carton	755-4894
CPSC - Francine Shacter	492-6557
OSHA - William Warren	523-7177
FDA - Kenneth Boyers	245-7740

6. Recommendations

- A. DOT with its Hazardous Materials Transportation Act should be invited to work with the group as the transportation of asbestos is of concern in the other agencies' regulatory development. Also close contact should be established with the Subcommittee to Coordinate Asbestos/Asbestiform Research of the DHEW Committee to Coordinate Toxicology and related programs within the Public Health Service.
- B. As the results of the various projects and studies become known, it appears that all four agencies have an interest in cooperation in the following areas: standard definitions of asbestos/asbestiform, importance of size and shape of asbestos fibers, analytical methodologies used in asbestos determinations, use of asbestos, substitutes for asbestos, labeling requirements, asbestos removal and disposal techniques and procedures, levels of environmental contamination, levels of human exposure, human body burden levels, economic impacts statements developed for regulatory purposes and for monitoring activities.

Benzene
Summary

1. Background

Benzene is an organic chemical known to cause or contribute to adverse health effects. An accumulation of scientific reports strongly suggest an increased incidence of leukemia in workers exposed to benzene. Recent occupational studies also demonstrate an increased incidence of chromosomal damage to workers exposed to benzene at concentrations lower than the 1977 occupational standards.

2. Issues

The main interagency matter that will have to be resolved is OSHA/EPA regulatory decisions and jurisdiction over gasoline marketing operations. An OSHA/EPA task force is studying the issue now.

3. Statutory Authorities

OSHA - Occupational Safety and Health Act
EPA - Clean Air Act as amended 1977
CPSC - Consumer Product Safety Act; Federal Hazardous Substances Act

4. Principal Actions/Schedule

2/78 - OSHA Promulgates Benzene Regulation
5/78 - CPSC Proposes a ban of benzene as an intentional ingredient or as a contaminant in consumer products at levels or .1% or greater (gasoline and solvents or reagents for laboratory use are exempt)
8/78 - EPA Finalizes Health Risk Assessment Documents
1/79 - EPA Proposes First Set of Benzene Regulations
Fall 79 - EPA Promulgates First Set of Benzene Regulation

5. Principal Contacts

OSHA - James Vail	523-7193
EPA - Richard Johnson	(919) 541-5355
CPSC - Stan Marrow	(301) 492-6557
FDA - Edward Seligman	(301) 496-4937

6. Recommendations

- A. Coordinate studies necessary to make regulatory decisions on the control of benzene exposures at service stations:
 - OSHA/EPA - Initiate study of the implication to benzene levels in gasoline of lead phase down regulations.
 - OSHA/EPA - Initiate study of the health effects of exposures to other toxic organics contained in gasoline.
- B. Initiate joint research through NCI, NIEHS and other research groups to develop insights into health effects of long-term exposures to low levels of benzene.
- C. Coordinate information on benzene content in solvents and the effectiveness of joint regulatory action.

Beryllium (Be)
Summary

1. Background

OSHA and EPA are concerned with acute and chronic forms of berylliosis, and potential carcinogenesis from inhalation of beryllium. EPA also regulates beryllium in aquatic environments.

Be is a potent enzyme poison especially where mg is a co-factor including mitosis. Unlike inorganic Pb, Be continues to be active in sites where it is stored and may have a long latent period before it manifests toxicity. Both of these properties are significant for potential carcinogenesis. Be has produced cancer in the respiratory tract of rats and monkeys following inhalation. Although "epidemiology" has not established carcinogenicity in humans, the incidence in two studies was greater than anticipated. The available data indicate that Be should be suspect as a carcinogen.

2. Issues

Whether Be is a human carcinogen.

3. Statutory Authorities

OSHA - Occupational Safety and Health Act
EPA - Clean Air Act
Federal Water Pollution Control Act

4. Principal Actions/Schedules (tentative)

1971 - OSHA Occupational Exposure Standard
1973 - EPA Final Emissions Standard
10/17/75 - OSHA proposed revision
1976 - EPA Water Criterion Standard
1977 - OSHA Hearings on revision
Summer, 1978 - EPA Revision to Water Criterion Standard

5. Agency Technical Contacts

OSHA - Robert Manware 523-7183
EPA - John Carroll 245-3042
Len Guarraia 245-3042

6. Recommendations

Routine mailings of technical and administrative publications, notices, etc; regular telephone contact to update on meetings, share agency indices on literature, contracts information staff assignments; support investigations of other agencies as to need for further regulation.

Cadmium
Summary

1. Background

Cadmium has a long biological half-life, accumulates in the liver and kidney, and is not known to serve an essential biological function. Damage to the renal tubules may occur at 200 ppm cadmium in the renal cortex. Exposure to cadmium dust may cause emphysema. Indications that cadmium may be a carcinogen, teratogen, and mutagen are of particular concern to the four agencies.

2. Issues

Is sufficient data available for exposure criteria and standard determinations? How adequate is the carcinogenicity, teratogenicity and mutagenicity data? Can no-effect levels and allowable daily intake levels be established for cadmium in foods? What are the contributions to total exposure from various sources, and do these levels pose risks to human health? How do we avoid increases of cadmium in environmental media and in the food chain? What are the alternatives to cadmium and the essential or safe uses of cadmium? Does cadmium have an essential biological function?

3. Statutory Authorities

CPSC - Federal Hazardous Substances Act; Consumer Product Safety Act.
FDA - Food, Drug, and Cosmetic Act.
OSHA - Occupational Safety and Health Act
EPA - Clean Air Act; Resource Conservation and Recovery Act; Federal Insecticide, Fungicide, and Rodenticide Act; Toxic Substances Control Act; Federal Water Pollution Control Act (currently in effect: water quality criteria, effluent guidelines for various industries, and spills regulations); Marine Protection, Research, and Sanctuary Act (Ocean dumping currently limited to trace amounts); Safe Drinking Water Act (current drinking water standard is 0.01 mg/l).

4. Principal Actions/Schedules (Tentative)

Fall 78 - EPA/FDA/CPSC Statement on cadmium and other heavy metals leached from decorated glassware
10/8/78 - FR notice on EPA air programs decision
12/78 - FR notice on proposed OSHA standards
Spring - Final decision on cadmium RPAR
1979

5. Principal Contacts

EPA - Elbert Dage 755-4894
Richard Johnson 8/629-5355 (FTS)

FDA - Samuel Shibko	472-5706
Frank Cordle	245-3114
CPSC - Joseph McLaughlin	245-1445
OSHA - George Ozga	523-7186

6. Recommendations

Coordinate exposure analyses; review waste disposal and food guidelines; review implications of carcinogenicity, teratogenicity, and mutagenicity data; review criteria data availability; review actions on decorated glassware; explain interagency differences in standards development; develop international data usage strategy; coordinate interagency information gathering activities; provide for monthly information exchange and activities status report.

Chloroform and Chlorinated Solvents
Summary

1. Background

A. Health Effects

The health effects of chloroform and chlorinated solvents include central nervous system and myocardial depressions, liver disfunction, and carcinogenic reactions. These chemicals are widespread and present a health problem in food additives, cosmetics, drinking water, various mechanical operations and air pollution. These chemicals present a possible health hazard in aerosols, paints, paint removals, lacquer thinner, degreasers and cleaners. Chloroform is also used as a pesticide and grain fumigant.

B. Production/Use

Chloroform - from controlled chlorination of methane; used as a solvent for fats, oils, rubber, alkaloids, waxes, gutta-percha, and resins; as a cleansing and/or degreasing agent; in fire extinguishers, in the rubber industry; as an anesthetic.

Methylchloroform - addition of HCl to 1,1-dichlorethylene; in metal cleaning and cleaning plastic molds; solvent in aerosols.

Trichloroethylene - passing tetrachlorethane vapor over calcium chloride catalyst at 300; solvent for fats, waxes, resins, oils, rubber, paints, and varnishes; degreasing; dry cleaning; analgesic and anesthetic; disinfectant and detergent for surgical instruments.

Perchloroethylene - catalytic chlorination of acetylene; dry cleaning; degreasing metals; solvent; and anthelmintic.

2. Issues

- A. Scope of chlorinated solvents - should carbon tetrachloride, ethylene dichloride, methylene chloride, vinylidene chloride be included in consideration of interagency exchanges?
- B. To what extent do methylene chloride, perchloroethylene and methyl chloroform actually pose a health hazard?
- C. What are the jurisdictional boundaries concerning these chemicals particularly in regard to water, and do they need clarification?
- D. Can the widely varying priorities each Agency has attached to its investigation and regulatory effort on chloroform and chlorinated solvents be resolved so that the most productive interagency action is not inhibited?

3. Statutory Authority

- FDA - Federal Food, Drug and Cosmetic Act
- EPA - Clean Water Act
 - Toxic Substances Control Act
 - Clean Air Act
- CPSC - Federal Hazardous Substances Act
 - Consumer Product Safety Act
- OSHA - Occupational Safety and Health Act

4. Proposed Actions/Schedules (Tentative)

A. FDA - Summer 1978

Methylchloroform (1,1,1-trichloroethane) §310.507 final rule. The document will amend the new drug regulations by adding a provision requiring an approved new drug application to market any aerosol drug products containing trichloroethane and intended to be inhaled either directly or indirectly.

Proposed rule to prohibit use of perchloroethylene (tetrachloroethylene) in human drug products because a study by NCI shows it to be carcinogenic in test animals.

Proposed rule to prohibit use of perchloroethylene (tetrachloroethylene) in adhesives and foamed polystyrene intended for food contact.

Final rule to (1) amend the color additive regulations by deleting trichloroethylene from list of permissible solvents in certain color additives; (2) amend the food additive regulations to delete provisions for use of trichloroethylene in the manufacturing of food and food contact surfaces.

- B. OSHA and CPSC have not initiated any regulatory actions at this time and no time table for their future actions is possible until they complete the assessment stage of consideration of these chemicals. Proposed interim primary drinking water regulations were published in the Federal Register (Volume 43, 28, Part II, p. 5756-5780) on February 9, 1978. These proposed regulations included trichloroethylene, methyl chloroform, and perchloroethylene. Under the proposed regulations, granular activated carbon treatment systems are to be used by all communities with populations greater than 75,000 to treat drinking water. Because of the multitude of organic contaminants that may be potentially present in a water supply, no specific limitations were placed on any of the three individual compounds.

5. Principal Technical Contacts

EPA - Dan Cirelli	755-2972
Pat Hilgard	755-2110
Bob Kellam	629-5355
Stan Mazaleski	755-6956
Alma Shea	755-8050
Charles Trichillo	472-6820
OSHA - Robert Cluck	523-7075
FDA - Carl Giannetta	472-6820
CPSC - Andrew Ulsamer	245-1445

6. Recommendations

- A. A determination of the proportion of chlorinated solvents in water, air, consumer products, and food should be made.
- B. As the results of ongoing contracts and studies come in, more meetings should be held so that regulatory considerations can be a joint effort.
- C. More discussion between the agencies should occur on the possibility of regulating chemicals by classes, specifically chlorinated solvents. At a minimum, methylene chloride must be considered with the four original chemicals.
- D. Members of industry or concerned consumer representatives might be invited to some regulatory work group meetings when regulatory matters concerning their industry are held.
- E. The work group should meet periodically to arrange for the exchange of data and planning for defining common needs and apportioning workloads.

Chlorofluorocarbons
Summary

1. Background

Continued release of chlorofluorocarbons is believed to lead to depletion of the stratospheric ozone layer. The reduction in stratospheric ozone will lead to an increase in the rate of skin cancer, possibly affect biological productivity, and possibly induce change in climate. In addition, accumulation of trichlorofluorocarbon and dichlorofluorocarbon may directly affect the climate through absorption of infrared radiation.

In October 1976, three Federal agencies (FDA, CPSC and EPA) formed the Interagency Chlorofluorocarbon Work Group. They agreed to pool their resources and work together to limit nonessential chlorofluorocarbon emissions. This interagency approach has developed an efficient and nonduplicative regulatory approach to nonessential aerosol uses of fully halogenated chlorofluoroalkanes. Phase I regulations were proposed jointly by the three agencies on May 13, 1977 and promulgated March 17, 1978. Initial introduction into interstate commerce of FDA-regulated products is prohibited after April 15, 1979.

2. Issues

The Interagency Work Group has started its investigation of nonpropellant chlorofluorocarbon uses (Phase II). These uses include refrigeration, air conditioning, foam blowing, solvents, chilling of foods, ethylene oxide sterilization diluent, and a variety of miscellaneous products. These uses are much more complex than the aerosol uses, and therefore the impact of nonaerosol regulation will be much greater than aerosol regulation principally due to the lack of good substitutes in a majority of the former uses.

OSHA has only recently become involved with the Work Group. The OSHA representative will be particularly helpful in the assessment of possible toxic effects resulting from the use of chemicals in the workplace which may become alternatives to chlorofluorocarbons.

3. Statutory Authorities

Aerosol propellant regulations:

FDA - Food, Drug, and Cosmetic Act, National Environmental Policy Act (NEPA)

CPSC - Consumer Product Safety Act

EPA - Toxic Substances Control Act

Nonpropellant regulations (should any be proposed):

EPA - Clean Air Act Amendments

FDA - May either defer to EPA under the Clean Air Act or regulate under the Food, Drug, and Cosmetic Act

CPSC - May either defer to EPA under the Clean Air Act or regulate under the Consumer Product Safety Act

4. Proposed Actions and Schedule

3/78 - Promulgate Aerosol Regulation
Early - Recommendation on the need of additional regulatory
1979 controls on known nonpropellant sources

5. Principal Contacts

EPA - George Wirth	426-9000
Ferial Bishop	755-8963
FDA - David Klauder	245-3459
CPSC - Colin Church	492-6731
Arlen Slobodow	492-6647
Dorothy Cantor	492-6744
OSHA - Bob Cluck	523-7076

6. Recommendation

Vigorously promote an international ban on chlorofluorocarbons for non-essential use as aerosol propellants.

Chromates
Summary

1. Background

A. Health Effects

Chromates are toxic to fish and invertebrates and toxic to activated sludge. In addition, chromates produce tumors in mammals, are irritants, corrosives, and cause skin ulcers and inflammation of the kidney.

B. Production/Use

Chromium (VI) is manufactured from chromite ore obtained primarily from the Republic of South Africa, Southern Rhodesia, and the USSR. Human and environmental exposure occurs from chromate production, and from its use in paint and primer pigments, fungicides, wood preservatives and corrosion inhibitors.

2. Issues

There are no issues of conflict between the agencies. In rulemaking, concerns will inevitably be raised concerning the degree of hazard and feasibility of proposed regulation.

3. Statutory Authorities

OSHA - Occupational Safety and Health Act
FDA - Food, Drug and Cosmetic Act
EPA - Federal Water Pollution Control Act

4. Principal Actions/Schedules (Tentative)

1971 - OSHA Initial Occupational Exposure Standard
1976 - EPA Drinking Water Standard, Water Quality Criterion
(Currently being revised)
1978 - OSHA proposed revision to Occupational Exposure Standard
1978 - EPA BAT revisions

5. Agency Technical Contacts

OSHA - Gerald Weinstein 523-9603
FDA - Gerald L. McCowin 472-5740
EPA - John Carroll 245-3042

6. Recommendations

At present, no agency is highly active in regulating chromates. As rulemaking progresses, however, technical contacts should receive mailings of technical and administrative publications, notices, etc. on a routine basis. Regular telephone contact to update meetings, and to share indices of literature, contacts, and staff assignments should also be maintained.

Coke Oven Emissions
Summary

1. Background

Coke oven emissions have been linked to lung cancer and other adverse health effects through epidemiological studies of occupationally exposed persons. On October 22, 1976, OSHA promulgated standards to limit worker exposure to Coke Oven Emissions (COE). These standards were promulgated for occupational worker protection and not for protection of the public. Ambient air monitoring in the vicinity of steel plants has shown high levels of benzo(a)pyrene (BaP), a carcinogenic constituent of COE. Therefore, EPA is pursuing a regulatory decision program for coke oven emissions.

2. Issues

- A. Whether EPA action will pre-empt OSHA action under Section 4(b)(1) of the Occupational Safety and Health Act of 1970?
- B. How to perform the health risk assessment and develop a regulation to deal with a mixture of pollutants rather than a single chemical species?
- C. How EPA's current review of its carcinogen regulatory policy may influence the nature and timing of the coke oven standard?

3. Statutory Authorities

OSHA - Occupational Safety and Health Act
EPA - Clean Air Act

4. Principal Actions/Schedules (Tentative)

Open - EPA will decide whether to list "Coke Oven Emissions" as a Hazardous Air Pollutant under Section 112 or as a New Source Performance Standard under Section 111, and will initially propose emission standards for wet-coal charging and battery topside leaks.

5. Principal Contacts

EPA - Justice Manning 8/629-5231 (FTS)
OSHA - Bob Cluck 523-7105

6. Recommendations

Continued coordination with OSHA and other EPA program offices.

Dibromochloropropane (DBCP)
Summary

1. Background

DBCP has been found carcinogenic in laboratory animals and induces adverse reproductive effects in animals and man.

EPA is considering restricting or cancelling the registered uses of DBCP. OSHA has established a permanent standard for occupational exposure. FDA has conducted sampling of food products. TRIS (a flame retardant) contained DBCP as a contaminant.

2. Issues

- A. Does EPA's proposed cancellation/restriction action give farmers and the public protection that is equivalent to the protection offered by OSHA's standard for pesticide plant workers?
- B. Do EPA and OSHA agree on the protective clothing and respirators recommended by EPA for certified applicators?

3. Statutory Authorities

EPA - Federal Insecticide, Fungicide and Rodenticide Act
OSHA - Occupational Safety and Health Act
FDA - Food, Drug and Cosmetic Act

4. Proposed Actions and Schedule

Continuous - Maintain informal contacts
3/15/78 - OSHA permanent standard issued
6/30/78 - Complete EPA's RPAR procedures

5. Principal Contacts

EPA - Jeff Kempter (lead) 755-8053
OSHA - David Welsh 523-7174
FDA - Paul Corneliussen 245-1152

6. Recommendations

None

Diethylstilbestrol (DES)
Summary

1. Background

DES is a synthetic estrogen and is currently being used in animals for both increased rate of gain and improved feed efficiency. DES as a human drug has been marketed as an orally administered effective and inexpensive non-steroidal synthetic estrogen. In humans, a statistically significant relationship has been identified between the administration of DES to pregnant women and the appearance of a rare type of cancer in daughters born of these pregnancies — adenocarcinoma of the vagina—and appearance of urogenital lesions in male offspring.

2. Issues

- A. The adverse effect on offspring prenatally exposed to DES may be a drug class effect applicable to estrogens as a class.
- B. In view of data from the Center for Disease Control (CDC), the pragmatic value of DES as a postcoital contraceptive for "emergency" use requires further evaluation.
- C. A "no effect" dosage level should be determined for those employees engaged in the manufacture or packaging of DES and its derivatives.
- D. The toxic health effects on employees engaged in the production and packaging of DES and estrogens should be assessed.

3. Statutory Authorities

FDA - Food, Drug and Cosmetic Act
OSHA - Occupational Safety and Health Act

4. Proposed Actions to Resolve Issues and Schedules

FDA is presently involved in a hearing to remove DES from the market as a drug used in animals. Both FDA and OSHA are reviewing and evaluating studies relating to human toxicity.

5. Principal Technical Contacts

FDA - Richard T. Hunt	443-3480
(Chairman)	
- Ridgely Bennett	443-3490
- Andrew J. Beaulieu	443-1846
- Edison Monk	443-1414
- Fred Degnan	443-4350
OSHA - Patricia Marlow	523-7148

Coordinators:

Ronald J. Wylie

443-3480

6. Recommendations

Determine if the effects observed for DES are a drug class effect applicable to estrogens as a class.

Ethylene Dibromide (EDB)
Summary

1. Background

EDB has been found to induce tumors, mutations, and reproductive effects in experimental animals. Its primary use is as a gasoline additive. It is also used as a fumigant, an industrial intermediate, and a solvent.

There is currently a workplace standard for EDB, which has been registered as a pesticide ingredient. OSHA is presently considering making the workplace standard more stringent and EPA is contemplating restriction of EDB's use as a pesticide.

2. Issues

- A. What is the degree of hazard associated with public exposure to EDB?
- B. Are the priorities that have been established by IRLG Agencies' regulatory programs consistent?
- C. What joint regulatory actions can reduce the hazards?

3. Statutory Authority

EPA - Federal Insecticide, Fungicide, and Rodenticide Act; Toxic Substances Control Act
OSHA - Occupational Safety and Health Act
FDA - Food, Drug and Cosmetic Act

4. Proposed Actions/Schedules (Tentative)

Continuous - Maintain strong informal contacts
1/78 - Rebuttal period for EPA's RPAR

5. Principal Contacts

EPA - Suzanne Harker (lead)	755-5687
OSHA - Flo Ryer	523-7174
FDA - Caesar Roy	245-1186

6. Recommendations

Assure exchange of data on any monitoring results, exposure estimates, the benefits of EDB use, and agency actions, meetings, and plans.

Ethylene Oxide (ETO) and Its Residues,
Ethylene Chlorohydrin (ETCH) and Ethylene Glycol (ETG)
Summary

1. Background

Recent corroborated evidence confirms that ethylene oxide (ETO), a common sterilant, and ethylene chlorohydrin (ETCH) are mutagens in test systems and thus potential human mutagens. In addition, a number of known local and systemic toxic effects in animals and humans are caused by or are associated with the use of ETO.

2. Issues

Equally safe practical substitutes for the ethylene oxide sterilization of some life sustaining and life saving products such as implanted medical devices, kidney machines and sterile disposables are not presently known. All pesticidal uses of ethylene oxide involve risk/benefit decisions which require the coordinated views of the IRLG agencies. Ultimate decisions should reflect the respective regulatory responsibilities.

EPA is currently evaluating the continued uses of ETO as a fumigant and sterilant. EPA's decisions will be based on the risks and benefits of each specific use situation as required by law. Each specific use involves particular concerns. FDA and CPSC will be assessing these particular concerns in accordance with the authorities outlined below. Development of this information, along with OSHA's general views of occupational exposure, will result in a more informed decision on the continued uses of ETO as a fumigant and sterilant and provide a basis for future regulatory actions.

3. Statutory Authorities

CPSC - Federal Hazardous Substances Act; Consumer Product Safety Act
EPA - Federal Insecticide, Fungicide, and Rodenticide Act; Toxic Substances Control Act
FDA - Food, Drug and Cosmetic Act
OSHA - Occupational Safety and Health Act

4. Schedule of Action (Tentative)

1/17/78	EPA - Published "Notice of Rebuttable Presumption Against Registration" of ETO.
5/15/78	- Rebuttal Period ended. ETO Working Group continuing with review. First objective is to obtain rebuttal material and determine whether presumption of risk was rebutted.
1/27/78	FDA - Published notice of intent to propose "interim maximum residue limits" and "interim permissible daily levels of exposure" for ETO, ETCH, and ETG.
3/78	- Plan to publish proposed "maximum residue limits" and "maximum daily levels" for ETO, ETCH, and ETG.
Open	OSHA- Conducting an assessment to regulate ETO through a generic pesticide standard on a generic standard for the standard completion program.

5. Principal Contacts and ETO Liaison Group Members

FDA	- Rosa M. Gryder (Chairperson)	443-4490
	Robert W. Barnes	443-1177
	Charles Kunkumian	443-4330
	Carl Bruch	427-7230
EPA	- Joe Boyd (Project Manager)	755-5632
OSHA	- Flo Ryer	523-7174
	Edith Godette	523-7166
CPSC	- Francine Schacter	492-6557

Regulations Development Work Group Coordinators:

Ronald J. Wylie	443-3480
Wayne A. Matthews	443-3480

6. Recommendations

- A. The IRLG agencies should continue to coordinate their scientific criteria-setting/rule-making activities and jointly evaluate the risk/benefit issues involved in restricting or prohibiting the use of ethylene oxide for particular products.
- B. Scientists should collaborate on the toxicity of ETO and the evaluation of data. There should, therefore, be a consistent and uniform approach to assessing risks and other key issues such as toxic dose, assumptions for human exposure limits, extrapolations from animals to levels of human exposure, etc.
- C. Enforcement issues should be resolved (e.g., inspections in hospitals and plants using ETO for sterilization) to make efficient use of inspector time and to avoid overlapping or conflicting regulatory actions. Jointly recommended guidelines for use should be developed.
- D. The ETO Work Group should reevaluate the utility of the ongoing and proposed scientific studies originally recommended by the 1973 FDA Ethylene Oxide Review Committee.
- E. Tier 4 mutagenicity studies on ETO should be initiated using I.P. or I.V. route of administration. A research geneticist at the National Center for Toxicological Research (NCTR), has tentatively agreed to do certain supplemental studies related to mutagenicity testing by the method of heritable translocation.
- F. Certain ETO teratological studies are being conducted at NCTR.

Lead
Summary

1. Background

Lead is an ubiquitous pollutant which affects several cellular biochemical activities at low levels and causes central nervous system disorders and brain damage at higher levels. Lead has been the subject of a number of Federal regulatory activities by the four IRLG agencies including: a proposed workplace air standard by OSHA; food and food container tolerances by the FDA; limitations in paint by the CPSC; joint deliberations by FDA, CPSC, and EPA on decorative overlays on glasses; a proposed ambient air standard by EPA; new source performance standards for lead-acid battery manufacturers; water quality criteria and effluent limitations by EPA; primary drinking water standards by EPA; and probably control over disposal of wastes containing lead by EPA. Other Federal programs relating to lead include programs by HUD to eliminate exposure to lead-based paint in residential dwellings and development of guidelines by the Center for Disease Control for screening children for lead poisoning.

2. Issues

- A. Determination of levels of lead within the body which result in adverse effects.
- B. Contribution of various sources of lead exposure to the total amount of lead in the human body.

3. Statutory Authorities

- EPA - Safe Drinking Water Act
- Federal Water Pollution Control Act
- Clean Air Act as Amended
- Federal Insecticide, Fungicide, and Rodenticide Act
- Toxic Substances Control Act
- Resource Conservation and Recovery Act
- OSHA - Occupational Safety and Health Act
- FDA - Food Drug and Cosmetic Act
- CPSC - Lead-Based Paint Poisoning and Prevention Act
- Federal Hazardous Substances Act
- Consumer Product Safety Act

4. Principal Actions/Schedules (Tentative)

- Four Agency participation in the EPA hearing on the proposed air standard
- A joint assessment of total lead exposure and health effects
- Information exchange and coordinated research
- Joint analysis of the combined economic impact of multiple regulatory actions on certain industries

5. Principal Contacts

EPA - Stan Coerr	8/629-5355 (FTS)
OSHA - Pat Marlow	523-7148
FDA - Pete Chichilo	472-5690
CPSC - Warren Potter, Jr.	245-1445

6. Recommendations

- A. Through the IRLG, the four regulatory agencies will endeavor to arrive at a joint position concerning the limits to total lead exposure consistent with a common goal for protection of public health, the relative significance of various routes of lead exposure, and the possible coordination of regulatory efforts. Participation in the IRLG group should be augmented with representatives of EPA/ORD, CDC, and HUD.
- B. The Federal agencies concerned with lead will exchange information on critical research findings in the scientific literature, as well as ongoing or contemplated agency funded research projects relevant to lead regulation.
- C. The four agencies will consider the feasibility of combined assessment of economic impact of multiple regulatory actions on certain industrial categories.
- D. Group discussions and information exchanges are of major value and will continue on a regular basis.

Mercury and Mercury Compounds
Summary

1. Background

The toxicity of mercury and its compounds has been well documented; these compounds have been the subject of a number of regulations by IRLG agencies. The main thrust of these regulatory actions have been to limit the levels of mercury in the environment and in food.

2. Issues

- A. An increase in the future use of coal could be associated with increased levels of mercury in the environment and in man.
- B. The health effects resulting from the use of mercury-containing compounds, as preservatives, in biologicals and multi-dose vials of human drugs should be reassessed to determine the level at which standards (maximum permissible levels) need to be established to reduce and minimize human exposure to mercury and its compounds.
- C. Additional research is needed to make a definitive assessment of the embryotoxic and fetotoxic effects of chronic exposure of women of childbearing age to low levels of mercury compounds, in view of reported maternal-fetal transfer mechanisms.
- D. Additional research is required to define sub-clinical effects resulting from chronic low-level exposure to mercurials.

3. Statutory Authorities

CPSC - Federal Hazardous Substances Act; Consumer Product Safety Act (Radium)
EPA - Safe Drinking Water Act; Toxic Substances Control Act;
Federal Water Pollution Control Act; Clean Air Act;
Marine Protection, Research, and Sanctuaries Act;
Federal Insecticide, Fungicide, and Rodenticide Act
FDA - Food, Drug, and Cosmetic Act
Public Health Service Act
OSHA - Occupational Safety and Health Act

4. Proposed Actions/Schedules (Tentative)

- A. The IRLG agencies propose to take a number of regulatory actions to reduce exposure to mercury and its compounds.
 - 8/78 - EPA determination of need to regulate under Section 4 of TSCA
 - 9/78 - EPA to publish water quality criteria for 65 chemicals including mercury
 - 2/79 - EPA will finalize water criteria for mercury
 - 12/78 - FDA will publish regulations on appropriate content of biological products

12/78 - FDA to publish proposed Tolerances for Mercury in Fish
1/79 - EPA determination of need to regulate under Section 6 and 7 of
TSCA

- B. Some specific uses of mercury will be eliminated such as mercury compounds used as pesticides except those for which adequate substitutes have not been found.
- C. Following a reassessment of mercury-containing preservatives used in biologicals and drugs, standards (maximum permissible levels) may be reestablished.
- D. Compatible Areas for Joint Regulatory Action:

OSHA regulations deal primarily with airborne mercury contamination problems in occupational settings. EPA is concerned with mercury in the environment (air and water) in addition to mercurial pesticides. FDA's interest lies in food (particularly in fish and shellfish), drugs, biologicals, and drug residues in animals. FDA shares the EPA concern for mercury contamination which may enter the food chain as well as in drug residues found in the edible tissues of food-producing animals. CPSC's concern is the use of mercury and mercury compounds in consumer household products. The concerns of the respective agencies should be coordinated and acted upon in a consistent and compatible manner. There are presently no identified areas of interagency conflict in the regulation of mercury and mercury compounds.

E. Possible Joint Actions:

(1) Exchange of Information - OSHA has provided the Mercury Work Group with a copy of their proposed revision in the "Occupational Exposure to Mercury" draft and a printout of case reports of occupational health effects associated with employees in plants manufacturing phenyl mercuric compounds.

(2) FDA/BD has provided the work group with data on possible embryotoxic effect of phenylmercuric acetate. In addition, FDA/BF will supply each of the other agencies with data from the Iraqi poisoning episode, as it is developed.

EPA has told the other agencies how to obtain copies of future EPA research projects.

(3) Sharing Expertise and Resources - The member agencies have been provided a copy of the development plan and the names of contact points in each agency. Information resources were exchanged. In addition, each agency has indicated a willingness to give testimony in hearings and other proceedings before other IRLG agencies.

The members have agreed to provide IRLG agencies with a list of their agencies' expert witnesses should the need arise.

5. Principal Technical Contacts

FDA - Dr. Samuel I. Shibko (Chairperson)	472-5705
Mr. Armond M. Welch	443-4960
Mr. John Wenninger	245-1530
Dr. John R. McDowell	443-5362
Dr. Mukund Parkhie (Alternative)	443-5362
Dr. Edward Seligmann	496-4937
Dr. Joan May	496-1853
EPA - Mr. James Kariya	755-1501
OSHA - Mr. Ching-Tsen Bien	523-7075
CPSC - Dr. Sam Molinas	492-6504
Regulatory Development Work Group Coordinators	
FDA - Mr. Ronald J. Wylie	443-3480

6. Recommendations

- A. That an assessment of the health impact of an increase in future use of coal (containing mercury and mercury compounds) be conducted with the cooperation of DOE and other energy agencies.
- B. The embryotoxic and fetotoxic effects of chronic exposure of women of childbearing age to low levels of mercury compounds be determined and tolerable levels of exposure be established.
- C. The sub-clinical effects resulting from chronic low level exposure to mercury compounds be determined, and used to establish tolerable levels of exposure.

Nitrosamines
Summary

1. Background

Many nitrosamines have been shown to be carcinogens in test animals and mutagens in selected bacterial test systems. They are very probably carcinogens in humans.

EPA is assessing the magnitude of the potential hazard of certain pesticides containing nitrosamines and is developing a policy with respect to nitrosamine-contaminated pesticides.

EPA has no current regulations regarding nitrosamines in air and is not planning any immediate regulatory action. EPA does have standards for nitric oxides in air based on health effects of the oxides and not on nitrosamines. The agency is, however, drafting a standard for nitrosamines in ambient water supplies.

On November 3, 1972, FDA proposed to eliminate all uses of nitrate in FDA regulated products, except home-cured products, all uses of nitrite as a color fixative, and certain uses of morpholine.

FDA is planning to withdraw its November 3, 1972 proposal regarding use of nitrates and nitrites and issue a new proposal requesting information on nitrosamines in certain foods.

A wide variety of cosmetic products are contaminated with N-nitrosodiethanolamine (NDELA) and possibly other nitrosamines. NDELA levels found in cosmetics range from 11 ppb to 130 ppm.

2. Issues

- A. Should action be directed only at nitrosamines per se or should standards be set for levels of the precursors: nitrates, nitrites, nitric oxides, and amines in air, water, and food?
- B. Are there tolerable levels for nitrosamines in air, water, and food or should exposure levels be set at zero? Due to the Delaney clause in the FD&C Act, FDA cannot set a tolerance based on risk/benefit analysis for a food additive which is a known carcinogen.
- C. Should EPA or FDA control levels of nitrosamines in water?

3. Statutory Authority

- A. FDA — Federal Food, Drug and Cosmetic Act (FD&C) Act

- B. EPA - Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
- Federal Water Pollution Control Act
- Clean Air Act

- C. OSHA - Occupational Safety and Health Act

4. Proposed Actions/Schedules (Tentative)

To maintain communication on nitrosamines, all relevant information forthcoming will be exchanged with concerned agencies. Whenever any regulatory action is initiated, the Agency contact will inform the other Agency contacts. Agency contacts will attend any critical meetings or hearings conducted by the other agencies. Each Agency contact will also provide the names of technical, legal and other interested informational people within the Agency to other Agency contacts.

A. EPA

- 2/78 - Proposed "National Ambient Air Quality Short Term Standard for Nitrogen Dioxide."
6/30/78 - Proposed standard for nitrosamines in ambient water supplies.

B. FDA

- Summer 1978 - Withdrawal of November 3, 1972 proposal regarding use of nitrates and nitrites and issuance of a new proposal requesting information on nitrosamines in certain foods.
Summer 1978 - Action on information received in response to request for data on nitrate and nitrites in poultry products (published September 2, 1977).
- Plan to issue notice that FDA is investigating the possibility that topically applied cosmetics contaminated with nitrosamines may be hazardous to human health.

5. Agency Technical Contacts

EPA	- John Bachmann	8/629-5231 (FTS)
	Martin Rogoff	426-2510
	Leonard Guarraia	245-3042
FDA	- Pete Chichilo	472-5690

6. Recommendations

- A. Because the impact of realistic exposure conditions of nitrosamines on human health has not been fully evaluated, it is recommended that the four agencies pool their knowledge and resources regarding nitrosamines in air, water, and food to determine whether there is a need for regulatory or control action relative to nitrosamines, and if so, what form this action should take.
- B. Analytical methods for determining nitrosamines should be further developed and validated among the agencies.
- C. The United States Department of Agriculture (USDA) should be included in further interagency contacts relating to nitrosamines.
- D. Policy decisions and statutory language should be clarified to clearly delineate FDA and EPA responsibility in regard to nitrosamines in water. This is necessary even while the agencies develop a consistent approach to this problem.

Ozone
Summary

1. Background

A. Health Effects

Ozone in air increases respiratory ailments. Other hazards are presently being assessed.

B. Production/Use

Ozone is an unwanted contaminant released during welding and as a result of electrical discharges. Secondary photochemical reactions cause its formation in the ambient air. Additionally, it is proposed that ozone be used in treating water.

2. Issues

- A. EPA currently has a standard for photochemical oxidants (measured as ozone) in the ambient air and OSHA currently has varying standards regarding the level of ozone that can cause health effects in airplanes.
- B. What priority has each agency attached to its investigation and evaluation of ozone?
- C. Jurisdiction over ozone in both water and air needs clarification.

3. Statutory Authority

FDA - Food, Drug, and Cosmetic Act
EPA - Clean Air Act
OSHA - Occupational Safety and Health Act

4. Principal Actions/Schedules (Tentative)

- A. FDA 1978 - Publish rule on affirmation of GRAS status of ozone for use as a disinfectant in bottled water.
- B. EPA Mid- - Review ozone Criteria Document (air) and propose
1978 revised standard. Proposal to set limit of trihalomethane in drinking water.
6/78 - Proposed ozone quality standard.
9/78 - Promulgation of ozone standard (air).

C. OSHA 9/78 - NIOSH - Preparation of Criteria Document.
Review of Document on Ozone Standard (air).

5. Agency Technical Contacts

EPA	- Mike Jones	629-5231
	J. Garner	629-2266
	Ervin Bellack	755-5643
OSHA	- Scott Merkle	523-7166
NIOSH	- Leela Murphy	513/684-8207
FDA	- Linda Taylor	472-4750

6. Recommendations

- A. Clarify jurisdictional questions between EPA and FDA concerning the regulation of substances to be used in the treatment of drinking water.
- B. Continue exchange of information.
- C. Include the Department of Transportation (DOT) in future discussions and attempt to resolve different standards enforced by DOT, EPA and OSHA on the level of ozone contamination in airplanes. (EPA does not have an ozone standard for airplanes; just an ambient air quality standard.)

Polybrominated Biphenyls (PBBs)
Summary

1. Background

In 1973, polybrominated biphenyls (PBBs) were mixed with cattle feed which was then distributed to a large number of farmers in Michigan. As a result, thousands of farm animals had to be quarantined and thousands more destroyed. Within four years of this incident the three farmer manufacturers of PBBs discontinued their production. The incident prompted considerable investigatory research and regulatory efforts.

2. Issues

Since PBBs are no longer manufactured, the primary issue is whether there is a need to regulate any of the PBB-related activities. A secondary issue is whether the EPA should take steps to control the risk of exposure to PBB from the resumption of the manufacture and processing of PBBs.

3. Statutory Authorities

EPA - Toxic Substances Control Act, Clean Air Act, Clean Water Act
OSHA - Occupational Safety and Health Act

4. Proposed Actions/Schedule (Tentative)

7/21/78 - Receive Reviewed Issue Paper and Draft I of Federal Register
Notice from AA/OTS
7/21/78 - Distribute Reviewed Issue Paper and Draft I of Federal Register
Notice to other Agencies and EPA Offices
8/25/78 - Obtain Comments on Issue Paper and Federal Register Notice
from other Agencies and EPA Offices
9/15/78 - Submit Final Issue Paper and Federal Register Notice to AA/OTS
9/29/78 - Submit Notice to Register Office
10/6/78 - Initiate the Writing of Section 8(a) Reporting Rule on PBBs

5. Principle Technical Contacts

EPA - Larry Dorsey	755-1188
CPSC - Joseph McLaughlin	245-1445
OSHA - Jackie Rogers	523-9225
USDA - John E. Spaulding	447-2807
NIOSH- Alexander Blair Smith	8/684-3593 (FTS)
FDA - Sidney Williams	245-1466
Frank Cordle	245-3114

6. Recommendations

A. Reporting Rule for PBBs

Since PBBs are no longer being manufactured, the hazard that formerly existed from PBBs no longer exists; therefore, there is no need at this time to control the manufacture, processing, or distribution in commerce of PBBs. If industry decided to resume the manufacture or processing of PBBs, however, health and the environment would be exposed to potentially hazardous new quantities of PBBs. For this reason, the work group is recommending that PBBs be subject to a TSCA, Section 8(a) Reporting Rule. This rule would require the notification in advance of the intent to manufacture, process, or import PBBs.

B. Substitutes for PBBs

Many of the substitutes for PBBs are structurally similar to PBBs. Since PBBs are known to adversely affect health and the environment, it is possible these substitutes may act likewise. Little toxicological information is available on these compounds. These structurally similar substitutes, therefore, have been recommended to the Interagency Testing Committee to be considered for a TSCA, Section 4 Testing Rule. This rule will require that manufacturers perform and report a series of specified toxicological tests on these compounds.

Polychlorinated Biphenyls (PCBs)
Summary

1. Background

Polychlorinated biphenyls (PCBs) are mixtures of the chemical compounds formed by the chemical bond of two benzene molecules into a biphenyl molecule with varying numbers of chlorine atoms attached to the biphenyl molecule.

Although PCBs have long been known to be toxic, only in recent years have they been acknowledged to be a general threat to the environment. They have been found in significant concentrations in waterways and sediments throughout the world. They are a widely spread contaminant of fish and wildlife resources. Recently, they have been identified in the milk of nursing mothers throughout the United States.

2. Issues

As the manufacture of PCBs has ceased, the major issues that remain to be resolved are use and environmental contamination. What uses, if any, should be permitted to continue? What level of PCBs is acceptable in foods? The issue of use is being addressed by an interagency work group. FDA has proposed lowering the existing guidelines for PCBs in certain foods.

3. Statutory Authorities

EPA - Toxic Substances Control Act
FDA - Food, Drug and Cosmetic Act

4. Proposed Actions/Schedule (Tentative)

2/78 - Promulgate Final EPA Regulation on Labeling and Disposal
Early 78 - Proposed EPA Ban Regulation
Early/Mid 78 - Final FDA Regulation on Food Levels
Late 78 - Final EPA Ban Regulation

5. Principal Technical Contacts

CPSC - Joseph McLaughlin	245-1445
EPA - Peter Principe	755-0920
FDA - Betty Campbell	245-3092

6. Recommendations

- A. Interagency coordination in the development of FDA and EPA regulations.
- B. Periodic sharing of all data, contract study outputs, and information.

Radiation
Summary

1. Background

The hazards associated with exposure to high levels of ionizing or nonionizing radiation are well established; however, the effects of low levels of exposure are not well defined and generally are difficult to determine. The principle of "As Low As Reasonably Achievable" (ALARA) is applied in most ionizing radiation protection programs based upon the conservative assumption that effects on the population may be directly proportional to the dose. Certain critics of this approach label it as overtly conservative, while others believe that it underestimates risks.

2. Issues

A. The scope of a national radiation protection program is so broad and involves so many agencies that it has been agreed to limit the scope of this plan initially to those areas which are more likely to involve two or more of the 4 agencies of the IRLG. Therefore, the plan emphasizes the following four areas:

- (1) Non-ionizing radiation
- (2) Occupational exposure
- (3) Radiation in the healing arts
- (4) Radioactive material in consumer products

B. There is a need for additional information on the biological effects of low levels of radiation especially with respect to light, micro-waves, and RF radiation and ultrasound.

3. Statutory Authorities

- CPSC - Consumer Product Safety Act
- Federal Hazardous Substances Act
- EPA - Atomic Energy Act
- Clean Air Act
- Federal Water Pollution Control Act
- Resources Recovery and Conservation Act
- Safe Drinking Water Act
- Marine Resources and Conservation Act
- Toxic Substances Control Act
- Solid Waste Disposal Act
- FDA - Food, Drug, and Cosmetic Act
- Public Health Service Act
- OSHA - Public Contract Act
- Occupational Safety and Health Act
- Contract Work Hours and Safety Act
- Longshoreman and Harbor Compensation Act

4. Proposed Actions/Schedules (Tentative)

A. Non-ionizing Radiation

1978 EPA - Exposure Guidelines
9/1/78 FDA - Phototherapy Guidelines
7/78 - Sunlamp Standard
9/78 - Mercury Vapor Lamp Standard
10/78 FDA - Microwave Diathermy Standard
7/15/78 - Diagnostic Ultrasound Guidelines
9/78 - Amendments to Laser Standard

B. Occupational Radiation

9/78 EPA, OSHA - Exposure Guidance
6/78 FDA, NRC, EPA, States - Suggested State Regulations

C. Ionizing Radiation in the Healing Arts

1978 EPA, FDA - Implementation of New Federal Guidelines
7/78 FDA - Recommendations Concerning Mammography Screening
9/10/78 - Recommendations on Quality Assurance in Dental Radiography
8/78 - Recommendation on Routine Chest Screening
9/78 - Recommendation on Diagnostic Examinations
5/1/78 - Recommendation on Use of Improved Intensifying Screens
9/2/78 - Recommendation for Utilization of Skull Radiography
5/79 - Recommendation Concerning Radiation Therapy
9/25/78 - Emergency Radiation Dose Limits for Health Care Personnel
8/78 - Recommendation on Nuclear Medicine Quality Assurance
12/78 - Recommendation on Nuclear Medicine Evaluation of Thyroid Gland
9/30/78 - National Standards for Medical Technologists
5/1/78, 7/1/78
8/1/78, 9/1/78 - Amendments to Diagnostic X-Ray Standard
8/1/78 - Recommendation for X-Ray Exposure of Women of Childbearing Age
5/78 - Recommendation for Quality Assurance in Diagnostic Radiology
7/78 - Recommendation for Post Treatment Dental Radiographs
9/78 - Recommendation Concerning Radiation Therapy for Benign Diseases

D. Consumer Product Radiation

12/30/78 FDA - Recommendation on Radioluminous Timepieces
- Guidelines or Standard for Smoke Detectors

5. Principal Technical Contacts

FDA - Ronald Wylie (Chairperson)	443-3480
Marshall Little	443-3429
Wayne Matthews	443-3480

EPA - Allen Richardson	557-8927
OSHA - David Lee	523-7179
CPSC - Alan Ehrlich	492-6498

6. Recommendation

- A. OSHA should consider initiating steps to revise its regulations concerning radiation protection to make these regulations consistent with new regulations of other Federal agencies (e.g., NRC), with new national guidelines, and with new radiation problems.
- B. The four agencies should assess the present data bases required for regulatory initiatives, especially with regard to the biological effects of low-level radiation (particularly non-ionizing) and should propose studies to fill any identified needs.

Sulfur Dioxide (SO₂)
Summary

1. Background

Sulfur dioxide is an irritant, increases the risk of respiratory disease, and is believed to promote lung cancer. These facts have been of concern to OSHA and EPA in their regulatory roles. FDA has generally regarded SO₂ as safe for use as a food preservative.

2. Issues

- A. Chronic effects of SO₂ exposure as a cancer promoter.
- B. Economic impact of SO₂ regulations.
- C. Reevaluation of SO₂ for use as a food preservative.

3. Statutory Authority

EPA - Clean Air Act
FDA - Food, Drug and Cosmetic Act
OSHA - Occupational Safety and Health Act

4. Principal Actions/Schedules (Tentative)

1971 - OSHA occupational exposure limit
10/25/71 - EPA National ambient air standard
10/75 - OSHA proposed revision to standard
1976 - FASEB evaluation as a food preservative
4/77 - OSHA hearings on proposed revision
1978 - OSHA final revision
1978 - EPA revision to emission limitations
1979 - FDA proposal for use as a food preservative
1980 - EPA Criteria Document revision expected

5. Agency Technical Contacts

OSHA - Patricia Waugh	523-7084
EPA - Jack Farmer	629-5471
CPSC - Stan Morrow	492-6557
FDA - Scott Andres	472-4750

6. Recommendations

Quarterly meetings to update technical representatives on the status of each agency's rulemakings.

Vinyl Chloride (VC) - Polyvinyl Chloride (PVC)
Summary

1. Background

A. Health Effects

Known carcinogen, possible mutagen, may be considered in relation to EPA pending cancer policy.

B. Current Regulatory Status

EPA - Proposed amendments to permanent standards for vinyl chloride emissions from manufacturing plants published 6/12/77.

FDA - Proposed 9/3/75 to prohibit rigid polyvinyl chloride (PVC) material for food contact use and to publish regulations establishing safe conditions of use for plasticized films and other prior-sanctioned uses of vinyl chloride polymers. Interested persons will be requested to submit current data to update files before final action is taken. A tentative final order concerning the use of rigid and semi-rigid PVC and another proposal concerning other uses will be published in 1978.

OSHA - Promulgated regulations setting permanent standards for vinyl chloride of 1 ppm averaged over an 8-hour period on 10/4/74.

CPSC - Promulgated revised regulation classifying self-pressurized household substances containing vinyl chloride as an ingredient or propellant as a banned hazardous substance (3/24/78).

2. Issues

A. Risk/Benefit - Due to the Delaney Clause, FDA cannot set a tolerance based on risk/benefit analysis for food contact use of a human carcinogen, though EPA and OSHA can.

B. Authority over PVC water pipe for potable water.

C. Opportunity for Joint Hearing - EPA and OSHA conduct hearings before promulgation of final regulations, FDA after promulgation.

3. Statutory Authority

EPA - Clean Air Act

FDA - Food, Drug, and Cosmetic Act

OSHA - Occupational Safety and Health Act

CPSC - Federal Hazardous Substances Act; Consumer Product Safety Act

4. Principal Actions/Schedules (Tentative)

3/24/78 - CPSC ban on use of VC as aerosol propellant

Spring 78 - EPA promulgation of amended final rule

- Open - FDA promulgation of amended final rule based on the proposal of 9/3/75
- 12/78 - FDA proposal concerning other uses of PVC in contact with food 12/78
- Open - OSHA updated Literature Search

5. Agency Technical Contacts

EPA - Susan Wyatt	8/629-5421 (FTS)
FDA - Gerard L. McCowin	472-5740
OSHA - Eugene Regad	523-7176
CPSC - Francine Shacter	492-6557

6. Recommendations

- A. Resolve the jurisdictional authority question for PVC water pipe between FDA, EPA, and CPSC or decide on joint action.
- B. Share any new data or information on vinyl chloride between the involved agencies. Circulate drafts of considered regulatory actions.
- C. Cooperate in joint development of economic and environmental assessment statements.

Waste Utilization or Disposal on Food Chain Land
Summary

1. Background

The health and environmental problems associated with wastes (e.g., sludge, wastewater, effluent, ground refuse, waste derived agricultural products, etc.) which are disposed or utilized on to food chain land are directly related to the quality of the waste, characteristics of the disposal site, application rate of the waste to the soil, and several other major management variables.

The work plan furthers the existing cooperation between FDA and EPA. For some time, FDA, EPA, and the U.S. Department of Agriculture have participated in an informal review process for rulemaking and policy documents. USDA continues to be an essential third party in this regard.

Working policies of FDA and EPA both acknowledge the value of using some wastes as soil conditioners or fertilizers. However, both agencies are also concerned that this utilization (disposal) be carefully managed.

2. Issues

- A. Close interaction among FDA, EPA, and USDA on this topic is essential for the development of a coordinated Federal program. Each agency's program supplements the other's areas of concern very well. The only potential conflicts foreseen are those related to specific wording and numerical limits used in final rules.
- B. CPSC and OSHA have decided, at present, not to participate in this interagency program. However, provision is made in the work plan for these agencies to become involved at any time and on any specific issue or review of any document. FDA and EPA should act to inform CPSC and OSHA of any item which is likely to be in their interest.

3. Statutory Authorities

FDA - Federal Food, Drug and Cosmetic Act
EPA - Clean Water Act
- Toxic Substances Control Act
- Solid Waste Disposal Act

4. Proposed Actions/Schedules (Tentative)

Early 1979 - Municipal Sludge Utilization and Disposal Regulations
Fall 79 - Home Use Bulletin
Spring 79 - Municipal Sludge Strategy (Final)
Early 1979 - Solid Waste Disposal Facility Regulations
Early 1979 - Landspreading Guidelines (Proposal)
Late 78 - Hazardous Waste Regulations (Proposal)
Open - Wastewater Treatment Regulations
Open - FDA Food Contaminant Levels

5. Agency Technical Contacts

EPA - Bob Tonetti 755-9120
FDA - George Braude 245-1152

6. Recommendations

The work plan established an interagency review process for rulemaking and major policy documents. It specifically recommends that when rule-making documents are submitted to Assistant Administrator review (EPA) or Associate Commissioner review (FDA), the comments received from the reviewing agency be attached to the rulemaking package. In effect, this action provides assurance that many issues will be resolved between the agencies prior to upper level agency review.

DEVELOPMENT PLANS

Acrylonitrile

1. Background

A. Health Effects

Acrylonitrile (AN) has long been known to be highly toxic if the vapor is inhaled or ingested, or if the liquid is absorbed through intact skin. Repeated skin contact with the liquid may cause dermatitis. Recent epidemiologic and animal studies have brought to light the potential additional hazard of acrylonitrile as a possible human carcinogen.

Acute Toxicity. The acute toxicity of AN has been fairly well documented in the literature and has been shown to vary widely among species. The reverse is, in fact true - "The findings of similar tumors in the inhalation and ingestion studies gives evidence of the apparently systemic nature of the carcinogenic effects of AN after absorption" (emergency temporary standard (ETS) p. 2589), also see review of all other studies under "Other Toxic Effects" #4 (pp. 2519-92 of the ETS, and especially the last paragraph of that section at the top of p. 2593). Human symptoms of overexposure to AN have included headache, dizziness, abdominal pain and vomiting, fatigue, asthenia, diarrhea and jaundice as well as some instances of convulsions. Acute intoxication resulting in death has been reported in a few cases.

Tumorigenicity/Carcinogenicity. In March of 1977, the Manufacturing Chemists Association (MCA) reported to OSHA and FDA the 12-month interim results of a 2-year study being conducted by the Dow Chemical Co. labs on the chronic toxicity of ingestion of AN by rats. Sacrifice of some of the animals after one year showed the development of various tumors, including central nervous system (c.n.s.) and ear canal tumors among treated animals, but not among the controls. The tumors were found in animals exposed to both 100 ppm and 300 ppm of AN in their drinking water. In April 1977, MCA reported further that similar tumors had been found in rats in the lowest exposure group, 35 ppm. The final report is expected in mid-1978 but may be delayed. In addition, a report of findings after one year of a continuing 2-year study of AN inhalation by rats noted comparable c.n.s. tumors in rats exposed to 80 ppm AN in air as well as a higher incidence of brain tumors (compared to historical controls) in those exposed to 20 ppm AN (see Ex 14-64) -- letter from the MCA to OSHA dated 2/22/78.

Mutagenicity. In addition, studies on the mutagenicity of AN have been conducted by several researchers employing a variety of methods. Of these, two showed completely negative results and the other three showed weak, but highly reproducible, activity. These form a consistent pattern in which the detectable mutagenic activity is dramatically increased when care is taken to control for the factors relating to volatility and levels at which toxic effects are demonstrated.

Teratogenicity. Evidence of a possible teratogenic effect of AN has also been evaluated. Data from two 1st generation litters of a 3-generation reproduction study conducted on Holtzman strain Sprague-Dawley rats indicated that the indices of fertility, gestation and

viability were significantly decreased at the highest level of AN administered (500 ppm in the drinking water). The offspring showed a growth retardation at the high dose level and the female rats on this dose level developed an unexpected progressive muscular weakness of the hind limbs 16-19 weeks following the weaning of the 2nd litter. In another study of the effects of AN on embryonal and fetal development, conducted at the Dow Chemical Research Laboratories, in which AN was given to pregnant Sprague-Dawley rats by gavage on days 6-15 of gestation, malformations and other signs of embryotoxicity at the highest levels (25 & 65 mg/kg.) were produced.

Human Epidemiological Studies. In May 1977, DuPont reported the primary results of an epidemiologic study demonstrating an excess of cancer among workers exposed to AN at a Dupont textile fibers plant in Camden, South Carolina. A cohort of 470 workers first exposed to AN in the polymerization operation between 1950 and 1955 showed 16 cancer cases occurring between 1969 and 1975 as compared with 5.8 cases expected (based on DuPont's rates). Of these 16 cases, 6 were lung cancers (compared to 1.5 expected), 3 were cancers of the large intestine (0.5 expected) and the remaining 7 were in 7 other primary sites. All of these cancer cases were found among the approximately 350 workers in the cohort first exposed to AN during the start-up of the plant between 1950 and 1952. In their report, DuPont stressed the preliminary nature of these results but noted that in light of recent animal tests, "(they) raise a serious suspicion that it (AN) may be a human carcinogen." CAG has advised that NIOSH has some information regarding the levels to which workers are exposed.

B. Production/Use

AN is a widely used chemical intermediary in the manufacture of acrylic fibers, synthetic rubbers and plastics. Approximately 1.5 billion pounds are produced annually in the United States. Most of this is used in the manufacture of a number of acrylic fibers and copolymer resins. Acrylic and modacrylic fiber production constituted 50% of the total AN consumption in the U.S. in 1976. Major producers of these fibers include American Cyanamid Co., Dow Badische Co., E.I. Dupont deNemours & Co., Eastman Kodak Co. and Monsanto Co. Acrylic fibers are used in the manufacture of apparel, carpeting, blankets, draperies and upholstery. Other major uses of AN include the manufacture of ABS (AN - Butadiene - Styrene) and SAN (Styrene - AN) resins and plastics, nitrile elastomers and latexes (rubbers) and other chemicals such as adiponitrile and acrylamide. AN is produced by the ammoxidation of propylene in the presence of a catalyst. Current producers of AN in the U.S. are American Cyanamid, DuPont, Monsanto and Vistron (SOHIO).

C. History and Current Status

OSHA. Occupational exposure to acrylonitrile had been limited to 20 parts of acrylonitrile per million parts of air, or 45 milligrams per cubic meter of air. This exposure limit was in terms of an eight-hour time-weighted average.

Because of the new evidence on the carcinogenicity of acrylonitrile, an emergency temporary standard (ETS) was issued by OSHA on 1/17/78. A proposed permanent standard was also published on that date. The ETS limited exposure to 2 ppm. Both included requirements for medical surveillance of exposed employees, environmental monitoring of the workplace, and an employee information program.

FDA. The Food and Drug Administration placed all acrylonitrile copolymers in an interim regulatory status on June 14, 1976 pending results of additional toxicology studies. In response to studies showing acrylonitrile monomer to be a mutagen, a teratogen and a tumorigen (2 year feeding study not as yet completed), FDA, on March 11, 1977, stayed all regulations concerning beverage bottles and proposed to lower the maximum allowable acrylonitrile monomer migration to 50 ppb.

On March 11, 1977 Monsanto Company obtained an injunction barring FDA from staying the regulation which permitted Monsanto to manufacture an acrylonitrile beverage bottle. Upon further deliberation the court ordered FDA to hold public hearings on the issue.

Hearings on acrylonitrile copolymer beverage bottles were completed on June 27, 1977. The initial opinion of the Administrative Law Judge upheld FDA's contention that the acrylonitrile beverage bottle was a food additive under the conditions of use and was not shown to be safe.

On September 19, 1977 the Commissioner of the Food and Drug Administration issued a final decision on the acrylonitrile copolymer bottle issue. The Commissioner upheld the Administrative Law Judge's initial opinion that the use of acrylonitrile copolymer bottles was a food additive situation and had not been shown to be safe under the conditions of use. The Commissioner's opinion published in the Federal Register of September 23, 1977 revoked the portion of the food additive regulations concerning acrylonitrile copolymer bottles (effective in 90 days) and continued the stay of these regulations until that time.

The Agency's existing proposal to limit all other uses of acrylonitrile copolymers to a 50 ppb extraction limit will be withdrawn and a new proposal will be issued for public comment. The new proposal will be more restrictive than the one currently outstanding.

EPA. EPA has a contractor doing a hazard assessment report on AN. In addition, EPA has initiated several monitoring programs through the OTS monitoring branch, the Research Triangle Park Air Office, and the Pollutant Strategies Branch, Strategies and Air Standards Division.

AN is also an EPA "Consent Decree" chemical, and one of 65 chemical classes over which the NRDC sued EPA to force regulatory action. EPA's Effluent Guideline Group is now monitoring AN, which will be covered under the Clean Water Act for best available technology for treatment at new facilities and for clean up at old facilities.

2. Issues

A. Degree of hazard

Decisions on the degree of hazard which AN's potential carcinogenicity and other possible hazards present will influence the scope and provisions of regulatory actions taken by the respective agencies.

A number of studies are ongoing to assess the toxicity of AN, including:

A two year rat feeding study sponsored by MCA which should be completed this year with the final pathology reports available by May 1978.

Monsanto studies of acrylonitrile metabolism and low-dose, long term toxicity which began in May 1977.

Dr. Maltoni's study of long-term acrylonitrile toxicity is now available.

NIOSH is assessing data on acrylonitrile for OSHA. The IRLG agencies have agreed to share all available data on this issue.

B. Economic Impact

The economic impact of possible new regulations will be a subject in these rulemakings and may influence to some degree the final decisions relative to the feasibility of the regulations. All four agencies are collecting data that will assist in evaluating this impact.

C. Regulatory Strategy

The members of the IRLG have the authority to regulate acrylonitrile from production and waste disposal through end use except for transportation. Given the hazards of this material, it is the responsibility of the IRLG agencies to develop a consistent and comprehensive "series of regulations" to address these hazards. A determination must be made as to which authorities will best provide this coverage.

3. Statutory Authority

- A. OSHA - Section 6(b) of OSH Act of 1970 (Authority and procedure for developing all health standards)
- B. FDA - Federal Food, Drug and Cosmetic Act
- C. EPA - Clean Water Act
Clean Air Act

- Federal Insecticide, Fungicide and Rodenticide Act
- Toxic Substances Control Act
- Safe Drinking Water Act
- Resource Conservation and Recovery Act
- D. CPSC - Consumer Product Safety Act; Federal Hazardous Substances Act

4. Principal Actions/Schedules (Tentative)

- 9/23/77 - FDA revoked food additive regs for use of AN to fabricate beverage containers
- 1/17/78 - OSHA issued proposed permanent standard and emergency temporary standard
- 1978 - FDA Environmental Impact Statement
- 1978 - FDA proposal to ban AN
- 1978 - EPA RPAR action
- 3/78 - OSHA Hearing on AN
- 1978 - OSHA Final Standard on AN

5. Agency Technical Contacts

OSHA - Gail Kleiner	523-9603
FDA - Thomas C. Brown	472-5690
EPA - Pat Hilgard	755-2110
CPSC - Glenn Simpson	492-6647
NIOSH - Sonia Berg	443-3680

6. Recommendations

A. Data in Hearing Records

Each agency develops extensive rulemaking records in support of regulation development. Duplication of effort can be reduced and a more comprehensive record established by sharing relevant data in the records. New information of probable interest will be routinely mailed to the technical staffs of the other IRLG agencies. It was suggested that those sections of the record too large for copying might be incorporated "by reference" in another agency's record.

B. Economic and Environmental Impact Assessment

The IRLG agencies can greatly benefit from shared data on both economic and environmental impact. In each of these reports agencies are looking largely at a common base of information on the economics of the industry. In the case of environmental impact statements, each agency should report the relationship of their action to other Federal agency efforts.

C. Periodic Updates

To establish a routine to assure that data is exchanged and that each agency is apprised of the status of every other agency's efforts,

copies of relevant new reports should be sent out at least monthly. Joint discussions of the status of rulemakings and any special problems should be held at least bi-monthly.

D. Analytical Methods

Practical analytical methods are essential to each agencies regulatory development and enforcement efforts. Each agency can benefit from sharing advances in analytical methods rather than independently developing new procedures and have agreed to share new analytical methods as soon as they are developed.

E. Contractor/Research Data

Each agency has been proceeding independently with contractors and in-house research to analyze hazard, develop production and use data, and study exposure levels in and outside the production site. Agency technical representatives should list and distribute all contractor efforts and in-house research on AN to the other technical group members. Information should include the contractor/agency office conducting research, objectives of effort, scheduled completion date or dates of interim reports and any reports produced to date.

F. Expert/Consultants

Each Agency should recommend agency experts or outside consultants who could be used as resource persons or expert witnesses during agency proceeding on AN.

Arsenic

1. Background

A. Health Effects

Arsenic may be absorbed by man through inhalation, ingestion or skin absorption. Any arsenic taken into the body is excreted primarily in the urine, feces, hair, nails, sweat, and epithelium. Arsenic may be found in small quantities in all the tissues including blood, bones, nails and hair. The toxic effects of inorganic arsenic compounds on man, following oral ingestion, are well known. Both acute effects (having a relatively severe course) and chronic effects (persisting over a long period of time) have been observed. Some of the effects of acute arsenic poisoning are: vomiting, nausea, diarrhea, irritation, inflammation and ulceration of the mucous membranes and skin, and kidney damage. Chronic inorganic arsenic poisoning results in dermatitis, muscular paralysis, visual disturbances, liver/kidney damage, suppression of the immunological system and neurological damage. Both acute and chronic poisoning by ingestion can lead to death; a lethal dose of inorganic arsenic is reported to range from 70 to 180 milligrams, although very few deaths each year are currently attributable to ingestion of arsenic.

Both external and internal injury may also result from air exposure to inorganic arsenic. Arsenic may be retained or absorbed in the lungs, although some inhaled material may be eventually cleared from the lung and swallowed. Most absorbed arsenic is rapidly excreted by the kidneys, but enough may remain to produce injury if intake is continuously high. Injury from air exposure is characterized by inflammation of the skin, nerve damage, and in severe prolonged cases, development of skin cancer. In advanced cases, damage to the liver and nervous system and decreased circulation of the fingers and toes may occur. The level of exposure which produces such effects is more frequently observed in occupational situations.

Experimental teratogenic effects of arsenic compounds have been reported, but none of the studies has been sufficiently exhaustive to allow accurate assessment of the human hazard. There is some evidence that arsenicals can be mutagenic in humans: an increased incidence of chromosomal aberrations was observed in cultures prepared from psoriasis patients who had been previously treated with arsenic.

There is strong epidemiologic evidence that inorganic arsenic is a skin and lung carcinogen in man. Skin cancer has occurred in association with exposure to inorganic arsenic compounds in a variety of populations, including patients treated with Fowler's solution, Taiwanese exposed to arsenic in artesian-well water, workers engaged in the manufacture of pesticides, and vintners using arsenic as a pesticide. The Taiwan data demonstrated a gradient of incidence with degree of exposure and age. All these populations had a pathognomonic sequence of skin changes leading to cancer.

Lung cancer has been observed to be associated with inhalation exposure to arsenic in copper smelters, workers in pesticide-manufacturing plants, Moselle vintners, Rhodesian gold miners, and residents near a pesticide plant producing arsenical. Two of the three smelter studies showed a gradient in the incidence of lung cancer with the degree of arsenic exposure; one of these studies also suggested that sulfur dioxide may be a carcinogenic co-factor for the lung. The case for arsenic as a liver carcinogen is not clear.

The absence of useful animal models is a serious handicap to the study of arsenic as a skin carcinogen and is probably due to metabolic differences between humans and the animals tested so far. The failure to induce skin cancer in test animals is perhaps not surprising, inasmuch as neither melanosis or keratosis has been duplicated in animals and these effects appear to be inseparably linked to the tumorigenic action of arsenic in the skin of man. The carcinogenicity of arsenic for the lung in animals has not yet been evaluated by inhalation studies.

B. Production and Use

Virtually all of the arsenic trioxide produced in the U.S. is recovered from copper, lead, and gold-bearing ores. The feed material includes arsenic-bearing ores originating mainly in the Butte, Montana and Coeur d'Alene, Idaho districts. Most come from concentrates from foreign mines or as flue dusts and speiss from other U.S. smelters. In 1975, all U.S. production and shipments were from the ASARCO plant in Tacoma, Washington. There is no secondary arsenic industry. To protect confidential company data, production and consumption figures have not been reported since 1959. U.S. consumption has been estimated as 22,300 kkg, with production of 8700 kkg. The balance of domestic demand was met by imports.

The 1974 demand for arsenic trioxide in the U.S. breaks down as follows:

Insecticides	23 percent
Herbicides (weed control)	24 percent
Dessicants and Defoliants	15 percent
Soil Sterilizers	18 percent
Wood Preservatives	6 percent
Animal Feed Activities	2 percent
Glass Additives	10 percent
Miscellaneous Uses	2 percent

C. Current Status of Regulations

EPA

EPA promulgated National Interim Primary Drinking Water Regulations for arsenic on December 24, 1975 of 0.05 mg/liter. These regulations are being reevaluated and promulgation of final standards is expected in the next few months.

Effluent guidelines for arsenic will be established for 21 major industries in the period 1979-1981.

A water criteria document on arsenic will be completed by June 1978 which will recommend a guideline level of arsenic for ambient waters based on health and welfare consideration of both aquatic and non-aquatic organisms (including man).

Under the Clean Air Act as Amended, EPA is evaluating the need to regulate arsenic. A decision on the need for regulation and the appropriate regulatory approach is scheduled for August 1978.

EPA is considering issuance of rebuttable presumptions against registration (RPAR's) for arsenical pesticides; a decision on issuance of RPAR's is anticipated by mid-1978.

OSHA

On May 5, 1978, OSHA promulgated a workplan standard of 10 ug/M³, 8-hour time-weighted average.

FDA

Regulatory action on arsenic is not currently under consideration, although additional food tolerances may be undertaken.

2. Issues

- A. The standards and regulations on arsenic in effect or being established by OSHA, FDA, and the various EPA programs are all health protection standards. Among these programs, there is not a consistent approach to determining the source of the arsenic body burden and the ultimate disposition of the arsenic, nor is there a common exposure model which can be used by the various agencies.
- B. Although there is strong epidemiologic evidence that inorganic arsenic is a skin and lung carcinogen in man, there is no animal model which has demonstrated this effect. It is unclear whether arsenic is teratogenic or mutagenic in man.
- C. A major issue affecting the regulation of arsenic emission sources and other sources of carcinogen emissions results from the inability to identify thresholds below which risk is minimized or eliminated. Thus, decisions on the degree of control which is necessary and appropriate, the source categories which should be controlled, and the scheduling and phasing of regulations are difficult. EPA has begun formulating a policy which will provide guidance on such decisions. This policy will form an important basis for the regulation of arsenic emission sources and will potentially affect the scope, degree, and timing of these regulations.

- D. OSHA has turned the jurisdiction for regulation of wood preservative use over to EPA's Office of Pesticide Programs. Clarification of EPA's role is needed to ensure adequate protection of workers and those using wood preservatives.
- E. EPA and FDA are in the process of reaching an agreement on the responsibility for regulations of substances (including arsenicals) which are both pesticides and animal drugs.
- F. Development of tolerances for arsenic in animals and in foods is an area where EPA's Office of Pesticides Programs and FDA could both provide data and reach agreement on appropriate goals for the tolerances, which are based on toxicity data. Possible issuances of rebuttable presumptions against registration (RPAR's) by the Office of Pesticides Programs will affect the development of arsenic tolerances by FDA and could result in lower or additional tolerances.

3. Statutory Authorities

EPA - Safe Drinking Water Act
 Federal Water Pollution Act
 Clean Air Act
 Federal Insecticide, Fungicide and Rodenticide Act
 Toxic Substances Control Act
 Resource Conservation and Recovery Act
 OSHA - Occupational Safety and Health Act
 FDA - Food, Drug and Cosmetic Act

4. Principal Actions/Schedules (Tentative)

A. EPA

- (1) Drinking Water. Under the provisions of the Safe Drinking Water Act, EPA promulgated National Interim Primary Drinking Water Regulations for arsenic on December 24, 1975. Effective on June 24, 1976 the regulations limit the concentration of arsenic in drinking water to 0.05 mg/l. In June 1977 the National Academy of Sciences (NAS) completed a report on the human toxicology of numerous compounds in drinking water, including arsenic. The report, which is to serve as the scientific basis for revising the interim drinking water regulations, concluded that the interim standard may not provide an adequate margin of safety in view of the association of arsenic in drinking water with incidence of skin cancer. EPA is reevaluating the interim arsenic drinking water regulation, and anticipates promulgation of the primary standard in the next several months.
- (2) Water Quality. The Federal Water Pollution Control Act allows EPA to establish effluent guidelines for waste streams from industrial facilities. Discharge of arsenic compounds is currently controlled under effluent guidelines for the metalloorganic pesticide (zero discharge), non-fertilizer

phosphates and boric acid production source categories. Arsenic is one of the 65 priority pollutants specified in the 1976 consent decree which requires the development of water quality criteria and the development of effluent guidelines for the specified pollutants from 21 major industries. The criteria for arsenic have been drafted; effluent guidelines for arsenic will be developed based on best available treatment technology ranging from arsenic concentrations of zero or no discharge to 0.05 mg/l.

- (3) Air Pollution. The 1977 Amendments to the Clean Air Act require that EPA evaluate the need for regulation of arsenic by August 7, 1978. Based on an evaluation of the 1976 National Academy of Sciences report on arsenic, EPA's Carcinogen Assessment Group concluded in April 1977, that "While arsenic has not yet been convincingly shown to be carcinogenic in animals, the evidence in humans is sufficient to warrant its being regarded as a carcinogen for regulatory purposes." In view of its adverse health effects, arsenic will likely be controlled under the Clean Air Act: a decision on the regulatory approach to control of arsenic is expected by August 1978. Regulations for control of arsenic emissions from process sources in the primary copper industries are being developed and depending on the regulatory decision, would be proposed by early 1979; the need for control of other sources will be evaluated and action taken as warranted. Based on a health assessment and population exposure study, the EPA Carcinogen Assessment Group has completed a preliminary risk assessment to estimate the risk associated with exposure to arsenic over a lifetime of exposure.
- (4) Pesticides Regulation. Under the Federal Insecticide, Fungicide, and Rodenticide Act (P.L. 92-516), EPA has granted registration to nearly twenty pesticide chemicals that contain organic or inorganic arsenic. At present, the Carcinogen Assessment Group is completing a preliminary health assessment as the basis for EPA's issuance of RPAR's for these products because of possible teratogenicity (for inorganic forms), mutagenicity, human carcinogenicity and neurotoxicity. RPAR's will be issued for each individual pesticide. A decision on the issuance of RPAR's is anticipated by mid-1978. Some arsenicals have been granted tolerances (allowable pesticide residues) for food crops although several tolerances have been cancelled in the past 10 years.
- (5) Toxic Substances Control. EPA could regulate arsenic under the provisions of the Toxic Substances Control Act if other regulatory authorities are not adequate to reduce population exposure; at present, action under this statute is not anticipated.

- (6) Solid Waste Control. Subtitle C of the Resource Conservation and Recovery Act of 1976 (PL 904-580) provides the authority for establishing a regulatory framework for controlling the management of hazardous wastes. Under Section 3001, criteria are currently under development to determine which solid and liquid wastes, such as those which contain arsenic, would be part of this hazardous waste management control system. Sections 3002, 3003, and 3004 mandate authority to establish regulations applicable to hazardous waste generators, transporters and owners and operators of hazardous waste treatment, storage, and disposal facilities, respectively.

Hazardous arsenic containing wastes would be a part of this "cradle to grave" regulatory system. The present schedule calls for final promulgation of such regulations by mid-1978.

B. OSHA

In January 1975, OSHA proposed a workplace standard for inorganic arsenic 4 ug As/m^3 , 8-hour time-weighted average. Since 1975, OSHA has been assessing available and new data on arsenic and developing the final standard based on the potential carcinogenicity of arsenic. The final standard is a technology forcing regulation based on the lowest level of technical feasibility determined by OSHA. The control strategy must employ engineering controls, improvement of work practice, and finally allow respirators for workers. Promulgation of the final workplace standard of 10 ug/m^3 , 8-hour time-weighted average occurred on May 5, 1978. NIOSH is scheduled to complete a Criteria Document on organic arsenic during 1979.

C. FDA

Arsenic is now used in veterinary medicine for non-food animals and as an approved food additive in swine and poultry. FDA's biggest concern is the use of arsenical herbicides for livestock forage since poisoning of livestock can occur. FDA has tolerances based on toxicity for arsenic in cotton hulls of 0.9 ppm As 203 , in kidney and liver of horses and cattle at 2.7 ppm As 203 and in meat, fat and meat products of cattle and horses at 0.7 ppm As 203 . Additional tolerances may be undertaken but have not been defined. Levels of arsenic in food products are evaluated under FDA's market basket survey but tolerances have not been established.

5. Agency Technical Contracts

EPA - Al Campbell	8/629-5231 (FTS)
Murray P. Strier	426-2560
Ervin Bellack	755-5643
Stan Coerr	8/629-5355 (FTS)
Bill Waugh	755-5851
Anita Schmidt	755-5851
Herman Gibb	755-5632

E.T. Merrick	755-4880
J. Howard Beard	755-9199
Paul Hoza	245-3030
Bob Carton	755-4894
OSHA - Gerald Weinstein	523-9604
FDA - John F. Brown	443-5362

6. Recommendations

A. Jurisdiction over Wood Preservatives

OSHA has given to EPA (Office of Pesticides Program) the jurisdiction over control of the use of wood preservatives. The Work Group recommends development of an issue paper delineating the scope of actions necessary and the appropriate regulatory approach to reducing arsenic exposure from wood preservatives. The objective of this action would be to ensure that workers in plants and individuals using products treated with wood preservatives are afforded adequate protection from exposure to arsenic.

B. Common Data Base and Information Exchange

The Work Group on arsenic recommends the development of a common data base on substances of mutual interest to the FDA, OSHA, CPSC, and EPA programs with regulatory responsibility. Such a program would be beneficial in encouraging a consistent approach to standard setting and a means of exchanging information expeditiously. Both FDA and EPA cite instances where data from other Agencies was difficult to obtain and required several weeks to retrieve.

C. Arsenic Body Burden Model and Hazard Assessment

Because human arsenic exposure comes from a variety of sources, the contribution of each source to body burden is significant for establishing meaningful regulations. The Work Group on Arsenic recommends the development of data on the source and disposition of arsenic in the human body, with a view of consistent regulatory goals among the FDA, OSHA, and EPA program offices. Establishing an interagency panel for assessing the hazards of arsenic compounds for human and animal health is also recommended.

D. Compliance and Enforcement

The Work Group on arsenic recommends joint plant visits as appropriate, either among the IRLG agencies or between EPA regulatory programs. When one Agency or EPA program plans to visit a plant of mutual concern because of arsenic, the other Agencies or programs should be notified so that if exposure data from various media could be obtained during the visit, arrangements to get such data may be made by the Agency in charge. As a part of this recommendation, FDA, OSHA, and EPA could prepare an issue paper on what kinds of exposure and plant investigations are possible under their respective statutes, what kinds of inspections are generally done and how the inspections can be expanded to serve the needs of other regulatory programs to avoid duplicating plant visits.

E. Health/Risk Assessment

EPA's Office of Air Quality Planning and Standards has requested a health/risk assessment from the Carcinogen Assessment Group, while the Office of Pesticides Programs has requested a preliminary assessment of the oncogenic potential of arsenic. The Work Group on Arsenic recommends that in the future, for pollutants of interest to several regulatory programs, a comprehensive health/risk assessment be completed for all media — not specific assessment of exposure for each route individually. The risk of exposure from the occupational setting and from media not covered by EPA programs should be included in the health/risk assessment.

F. Monitoring

A consistent approach to monitoring for environmental pollutants should be developed where feasible for comparability of data and consistent evaluation of levels of the pollutant detected. This is an area where the programs within EPA and the other Agencies could better coordinate their regulatory and enforcement activities.

Asbestos

1. Background

A. Health Effects

Asbestos or asbestiform minerals include several types or groups of fibrous crystalline substances with high tensile strength and special thermal and electrical properties. Their occurrence as pollutants in the ambient air and in food and drinking water has caused considerable concern because occupational exposures to asbestos in air have been found to induce asbestosis, cancer of the lung, mesothelioma of the pleura, mesothelioma of the peritoneum, and cancer of the intestinal tract after latent periods of about 20 to 40 years. Asbestos diseases have resulted from non-occupational exposure.

B. Production/Use

Asbestos is used extensively in the manufacture of such products as roofing, insulation (thermal and electrical), asbestos cement pipe and sheet, flooring, packing and gaskets, friction materials, coatings and compounds, plastics, textiles, and paper.

C. History and Current Status

(1) EPA

(a) Clean Air Act

- 36 FR 5931 (3/31/71) Notices List of Hazardous Air Pollutants (Asbestos)
- 36 FR 23239 (12/7/71) Proposed Rulemaking, Proposed Standards for Asbestos, Beryllium, and Mercury
- 38 FR 8820 (4/6/73) Rules and Regulations, Emission Standards for Asbestos, Beryllium, and Mercury (Milling, manufacturing, demolition, spraying, and roadways)
- 39 FR 15396 (5/3/74) Rules and Regulations, Emission Standards for Asbestos, Beryllium, and Mercury (Clarification of regulations)
- 39 FR 38064 (10/25/74) Proposed Rules, Proposed Amendments to National Emission Standards for Asbestos and Mercury (Shotgun shells, asphalt concrete, insulation, demolition, and waste disposal)
- 40 FR 48292 (10/14/75) Rules and Regulations Amendments to Standards for Asbestos and Mercury (Demolition, renovation, and waste disposal)
- 42 FR 12122 (3/3/77) Proposed Rules, Proposed Amendments to Asbestos Standard (Demolition and renovation)
- 42 FR 12127 (3/2/77) Rules and Regulations, Amendment to Asbestos Standard (Demolition and renovation)
- 42 FR 58523 (11/10/77) Advance Notice of Proposed Rulemaking, Development of Asbestos Standard for the Production and Use of Crushed Stone

(b) Federal Water Pollution Control Act

- 38 FR 1624 (1/16/73) Notices List of Categories of Sources (Asbestos)
- 38 FR 24342 (9/7/73) Rules and Regulations List of Toxic Pollutants (Asbestos)
- 38 FR 29944 (10/30/73) Proposed Rules Point Source Category, Effluent Guidelines (A-C pipe and sheet and asbestos paper, millboard, roofing products, and floor tiles)
- 39 FR 7526 (2/26/74) Rules and Regulations Point Source Category (A-C pipe and sheet and asbestos paper, millboard, roofing products, and floor tiles)
- 39 FR 7534 (2/26/74) Proposed Rules Point Source Category, Application of Effluent Limitations Guidelines for Existing Sources to Pretreatment Standards for Incompatible Pollutants (A-C pipe and sheet and asbestos paper, millboard, roofing products, and floor tile)
- 39 FR 31592 (8/29/74) Proposed Rules Point Source Category (Asbestos textiles, solvent recovery, vapor absorption, and wet dust collection)
- 40 FR 1874 (1/9/75) Rules and Regulations Point Source Category (Asbestos textiles, solvent recovery, vapor absorption, and wet dust collection)
- 40 FR 1879 (1/9/75) Proposed Rules Point Source Category, Pretreatment Standards for Existing Sources (Asbestos textiles, vapor absorption, and wet dust collection)

(c) Toxic Substance Control Act

- 42 FR 39182 (8/2/77) Proposed Rules General Provisions and Inventory Reporting Requirements; Supplemental Notice; Public Meeting (Asbestos)
- 42 FR 64572 (12/23/77) Rules and Regulations Inventory Reporting Requirements (Asbestos)

(d) FIFRA

(2) CPSC

(a) Consumer Product Safety Act

- 16 CFR - 1500.17(2)(7) - Bans Garments with Abestos
- 42 FR 38782 (7/29/77) Proposed Rules - Proposed Rules to Regulate Consumer Patching Compounds and Artificial Emberizing Materials Containing Respirable Free-Form Asbestos, Under the Consumer Product Safety Act
- 42 FR 38783 (7/29/77) Proposed Banning Rules - Proposal to Ban Certain Patching Compounds and Artifical Emberizing Materials Containing Respirable Free-Form Asbestos
- 42 FR 63354 (12/15/77) Rules and Regulations Regulation of Products Subject to Other Acts Under the Consumer Product Safety Act. Consumer Patching Compounds and Artificial Emberizing Materials Containing Respirable Free-Form Asbestos

42 FR 63354 (12/15/77) Rules and Regulations
Consumer Patching Compounds and Artificial Emberizing Materials
Containing Respirable Free-Form Asbestos. Establishment as
Banned Hazardous Products

- (b) Federal Hazardous Substances Act
Sections 2(p), 2(q)(1)(B), 3(a), 3(b)

(3) DOT

Hazardous Materials Transportation Act

41 FR 53824 (12/9/76) Proposed Rules
Environmental and Health Effects Materials. Advanced Notice of
Proposed Rulemaking (Potential inclusion of asbestos
as a regulated material)

(4) FDA

Federal Food, Drug, and Cosmetic Act

37 FR 3645 (2/18/72) Proposed Rulemaking
Asbestos-Containing Garments for General Use; Proposed Classi-
fication as Banned Hazardous Substance
37 FR 14872 (7/26/72) Rules and Regulations
Asbestos-Containing Garments for General Use; Classification
as Banned Hazardous Substances
37 FR 16407 (8/12/72) Proposed Rulemaking
Proposal Regarding Regulation of Prior-Sanctioned Food Ingredients
(Talc for use in coating polished rice)
38 FR 27076 (9/28/73) Proposed Rules
Asbestos Particles in Food and Drugs (Asbestos filters and talc)
40 FR 11865 (3/14/75) Rules and Regulations
Asbestos-Form Particles in Drugs for Parenteral Injection
(Asbestos filters)
40 FR 26683 (6/25/75) Proposed Rules
Electrolytic Diaphragm Process for Salt, Proposed Revocation
(Asbestos levels in salt)
41 FR 3286 (1/22/76) Rules and Regulations Electrolytic Diaphragm
Process for Salt, Revocation (Asbestos levels in salt)

(5) MESA

(a) Federal Metal and Nonmetallic Mine Safety Act

38 FR 7822 (3/26/73) Notices
Metal and Nonmetallic Mine Health and Safety Symposium on
Talc Dust Hazards. Notice of Public Meeting
38 FR 23383 (8/29/73) Proposed Rules
Proposed Health and Safety Standards: Metal and Nonmetallic
Open Pit Mines; Sand, Gravel, and Crushed Stone Operations;
Metal and Nonmetallic Underground Mines (5 fibers/cc, 8-hr
TWA airborne concentration of asbestos)
39 FR 24316 (7/1/74) Rules and Regulations
Health and Safety Standards: Metal and Nonmetallic Open
Pit Mines; Sand, Gravel, and Crushed Stone Operations; Metal
and Nonmetallic Underground Mines (5 fibers/cc, 8-hr TWA
airborne concentrations of asbestos)

42 FR 35000 (7/7/77) Proposed Rules

New and Revised Health Standards (Potable water, use or storage of toxic substances, and 8-hr TWA airborne concentration of asbestos)

(b) Federal Coal Mine Health and Safety Act

37 FR 23645 (11/7/72) Proposed Rulemaking

Coal Mine Health and Safety. Notice of Proposed Rulemaking (2 fibers/cc, 8-hr TWA airborne concentration of asbestos)

39 FR 13003 (4/10/74) Proposed Rules

Coal Mine Health and Safety. Notice of Objections Filed and Hearing Requested on Asbestos Dust Standard for Surface Work Areas of Underground Coal Mines and Surface Coal Mines.

39 FR 28176 (8/5/74) Notices

Asbestos Exposure in Surface Coal Mines and Surface Work Areas of Underground Mines; Findings of Fact

41 FR 10223 (3/10/76) Rules and Regulations

Surface Work Areas of Underground Coal Mines and Surface Coal Mines. Exposure to Asbestos (2 fibers/cc, 8-hr TWA)

(6) Occupational Safety and Health Administration

(a) Occupational Safety and Health Act

36 FR 10466 at 10506 (5/29/71) Rules and Regulations
Occupational Health and Environmental Control. Air Contaminants (Gases, Vapors, Fumes, Dust, and Mists) (12 fibers/cc airborne concentration of asbestos)

36 FR 23207 (12/7/71) Rules and Regulations
Emergency Standard for Exposure to Asbestos Dust (5 fibers/cc, 8-hr TWA)

37 FR 466 (1/12/72) Proposed Rulemaking
Standard for Exposure to Asbestos Dust (5 fibers/cc, 8-hr TWA)

37 FR 11318 (6/7/72) Rules and Regulations
Standard for Exposure to Asbestos Dust (Effective 7/7/72: 5 fibers/cc, 8-hr TWA; effective 7/1/76: 2 fibers/cc, 8-hr TWA)

40 FR 47652 (10/9/75) Proposed Rules
Occupational Exposure to Asbestos (0.5 fibers/cc, 8-hr TWA)

41 FR 11504 (3/19/76) Rules and Regulations
Occupational Safety and Health Standards. Standard for Exposure to Asbestos

2. Issues

The most critical need of all the agencies is for specific health effects decisions and/or research so the controversy with respect to the consequences of inhalation and ingestion of asbestos and asbestiform fiber can be resolved.

3. Statutory Authorities

- EPA - FIFRA
 - Clean Air Act, Section 112
 - Federal Water Pollution Control Act, Sections 307(a) and 304(b)
 - Toxic Substances Control Act, Section 6
 - Resource Conservation and Recovery Act, Subtitle C - Hazardous Waste Management
- CPSC - Consumer Product Safety Act, Section 8, 12, 15
 - Federal Hazardous Substances Act, Section 2(p), 2(q)(1)(B), 3(a), 3(b)
- FDA - Food, Drug and Cosmetic Act, Sections 402, 406, 409, 501, and 601
- OSHA - Occupational Safety and Health Act, Sections 6B, 6C, and 8C

4. Principal Actions/Tentative Schedules

- A. EPA's Office of Toxic Substances is preparing a preliminary assessment of the environmental exposure to asbestos fibers. This report will provide the basis for EPA's Priorities Committee evaluation of the need for further regulatory action either under TSCA or other authorities, or for further investigations.
- B. EPA and FDA participated in the protocol development of the NIEHS oral asbestos studies in rats and hamsters. This study is a systematic attempt to assess the biological effects associated with primary ingestions of chrysotile - long and short fibers, amosite, non-fibrous tremolite and crocidolite fibers. EPA contributes about 10% to the funding of this NIEHS program.
- C. Asbestos as a water pollutant is being surveyed by EPA in four areas: Seattle, San Francisco, Duluth and Connecticut.
- E. EPA is investigating the use of asbestos in pesticides.
- F. EPA is considering Asbestos as a hazardous waste under the Resource Conservation and Recovery Act.
- G. The Office of Toxic Substances (OTS) is currently attempting to confirm reported levels of amphibole fibers in the urine of residents from the western Lake Superior areas as well as the detection of chrysotile in urine samples from Minneapolis residents. OTS' contractor

the American Public Health Association (APHA) has formed an Advisory Panel to assess the significance of this report. APHA and OTS are currently identifying populations which may be suitable for urine monitoring studies.

- H. FDA awarded a contract to Structures Probe, Inc., on August 1, 1977 for methodology development to measure asbestos in foods, drugs and talc. The contract was initially let for one year, but it will probably have to be extended in order to produce methods suitable for regulatory purposes.
- I. FDA contracted with International Research & Development Corp., for a toxicological study of intravenously administered asbestos in rats and mice. The project was begun June 28, 1974 and should be completed by June 30, 1979.
- J. CPSC has completed a study to determine the extent to which asbestos is used in consumer products and is currently evaluating the need for further regulatory action.
- K. CPSC is investigating the feasibility of removal or coverage of sprayed asbestos ceilings in existing structures.

5. Agency Technical Contacts

EPA - Bob Carton	755-4894
CPSC - Francine Schacter	492-6557
OSHA - William Warren	523-7177
FDA - Kenneth Boyers	245-7740

6. Recommendations

- A. DOT, with its Hazardous Materials Transportation Act, should be invited to work with the group as the transportation of asbestos is of concern in the other agencies' regulatory development. Also close contact should be established with the Subcommittee to Coordinate Asbestos/Asbestiform Research of the DHEW Committee to Coordinate Toxicology and related programs within the Public Health Service.
- B. As the results of the various projects and studies become known, it appears that all four agencies have an interest in cooperation in the following areas: standard definitions of asbestos/asbestiform, importance of size and shape of asbestos fibers, analytical methodologies used in asbestos determinations, use of asbestos, substitutes for asbestos, labeling requirements, asbestos removal and disposal techniques and procedures, levels of environmental contamination, levels of human exposure, human body burden levels, economic impact statements development for regulatory purposes and monitoring activities.

Benzene

1. Background

A. Health Effects

In the June 8, 1977 Federal Register, EPA published its decision to list benzene as a hazardous air pollutant under Section 112 of the Clean Air Act (CAA). As indicated in that notice, an intensive health risk analysis was conducted with full public participation. As a result of this assessment, the Agency has concluded that a regulatory program should be undertaken to reduce general public exposures to benzene emissions. The Agency has tentatively concluded that regulations are needed for the manufacture of malaic anhydride and the distribution system for gasoline.

Benzene is an organic chemical known to cause or contribute to adverse health effects. Scientific reports strongly suggest an increased incidence of leukemia in workers exposed to benzene. Recent occupational studies demonstrate that benzene exposure is also causal to damage to chromosomes of exposed workers. In response to these data, NIOSH recommended to the Department of Labor in September of 1976 that current occupational standards for benzene be tightened considerably. In April 1977, NIOSH published a study indicating high levels of leukemia in workers exposed to benzene alone. This was the first study of its kind implicating benzene alone and the first study of its kind implicating benzene alone in the workplace as the potential cause of observed leukemia. Due in part to this study, and the accumulation of evidence of benzene's toxicity, on May 27, 1977, OSHA issued emergency temporary standards for workplace exposures and on February 10, 1978, OSHA promulgated final standards.

The observed levels of benzene in the workplace where increased incidences of leukemia have resulted are considerably higher than those levels present in ambient air. However, in proximity to certain sources the public may be exposed to excessive ambient levels on a continuous basis while workplace exposures are essentially 8 hours per day, 5 days per week. Thus, considerable uncertainty exists regarding the significance of observed ambient levels. As a result of this uncertainty, EPA conducted an intensive study of the potential risk of ambient levels around sources of atmospheric benzene. This health risk assessment was subject to review by the public and the EPA Science Advisory Board (SAB). Following the completion of that review assessment, the documents were judged adequate pending certain revisions which will be completed by August.

B. Production/Use

The bulk of the U.S. supply of benzene is extracted from refinery processing streams. In addition, a small amount of the national production (less than 10%) is produced as a by-product during the production of coke. Over 50% of the benzene produced is used as a gasoline component. Thus, gasoline-powered motor vehicles represent the largest source of benzene emissions.

Although they are the largest sources both in terms of numbers as well as total emissions, because they are so geographically dispersed, their resulting impact on atmospheric levels is considered to be significantly smaller than many other sources of benzene. Recent modeling for center city highway benzene concentrations using a variety of scenarios most favorable to atmospheric loading demonstrate that the impacts of benzene from motor vehicles are generally much lower than from certain stationary sources.

Large quantities of benzene are used as a raw material in the manufacture of organic chemicals such as maleic anhydride, ethylbenzene, nitrobenzene, cyclohexane, chlorobenzene and others. Benzene is emitted principally from reactor/exhaust vents, from fugitive leaks and during storage and handling operations. Control has already been accomplished to some degree through State and local regulations, and because benzene is a valuable commodity.

C. Current Status Benzene Regulation

(1) Decision to List Benzene. The decision to list benzene as a hazardous air pollutant under Section 112(b)(1)(A) was the result of an accumulation of evidence that exposure to benzene is related to an increased incidence of leukemia, aplastic anemia and other serious irreversible blood disorders in humans. Since benzene exposures have been shown to result in an increased incidence of leukemia and since no ambient air quality standard has been promulgated for it, benzene clearly satisfies the criteria for a hazardous air pollutant as defined in Section 112(a)(1) of the Clean Air Act, as amended, August 1977.

Listing benzene as a hazardous air pollutant under Section 112 will result in more expeditious control than would implementation of Sections 108, 109, and 111 which allow substantially more time to effect emission reductions. Also, the decision to list under Section 112 and not Sections 108 or 109 is supported by the strong suspicion that emissions from certain sources represent a potentially greater risk to public health than emissions from other sources.

As indicated in the Federal Register notice of June 8, 1977, previous Agency experience with regulations of vinyl chloride suggests that the required 180 days from listing of the compound to date of proposed regulations will not be feasible. More than 180 days will be required.

(2) Regulatory Alternatives. EPA has a wide range of regulatory authorities which could be used in place of or in addition to Section 112. The Toxic Substances Control Act (TSCA) is being considered for possible regulation of the benzene content of gasoline and as a way to prohibit the use of benzene in consumer products and industrial chemicals.

In addition, certain sources which do not warrant the development of 112 regulations will be given high priority in developing 111

regulations. For example, EPA's current program to develop New Source Performance Standards for chemical manufacturing facilities will also evaluate those benzene sources which may be potential candidates for 112 regulations; where applicable, supporting information for NESHAPS will be documented. The Agency is preparing a Federal Register Notice which discusses how the Agency views the implications of the health risk assessment and how the Agency intends to approach the regulation of sources. This Notice is expected to appear in the Federal Register by the middle of September.

(3) Health Risk Assessment. The health risk assessment for which EPA's Office of Research and Development (ORD) has responsibility, is the cornerstone of the Agency's regulatory decisions regarding which sources to control and the extent of control needed. Basically, this assessment provides estimates of the total incidence of leukemia which could be expected to result from benzene emissions from specific sources at specific locations as well as aggregate sources (i.e., all petroleum refineries). Additionally, estimates will be developed regarding implications of the use of control technology to reduce incidences. From these two types of estimates, a priority is being developed for each source category.

To estimate incidences of leukemia, essentially three pieces of information will be needed. They are:

1. Benzene concentrations in the vicinity of sources,
2. Estimates of the population living in the vicinity of the sources, and
3. A risk rate coefficient which relates leukemia incidence to benzene exposure levels.

Items 1 and 2 were developed by Stanford Research Institute (SRI) in conjunction with Strategies and Air Standards Division (SASD). Item 3, the risk rate coefficients, were developed by ORD's Cancer Assessment Group (CAG). The CAG's coefficients are to be applied to SRI exposure estimates to obtain total incidence. The third report of the health risk assessment is a review of the toxicity of benzene inhalation conducted by Dr. Leonard Goldstein of New York University.

These three reports were released for public review and comment in November 1977 and EPA held public meetings of its Science Advisory Board in December 1977 and again in February 1978 to discuss them. Based on consideration of the comments submitted and the recommendations of the Science Advisory Board, the Agency has revised the three reports and expects to have them available for release to the interested public by mid-August 1978.

(4) Methodology. A report of benzene emissions has been prepared by PEDCo. The report indicates that benzene emissions can be grouped

into seven major source categories: (1) motor vehicles, principally gasoline fueled; (2) gasoline marketing; (3) storage of gasoline, crude oil, benzene, and benzene-rich liquids; (4) petroleum refineries and other petroleum-related benzene production facilities; (5) coke ovens; (6) organic chemical manufacture; and (7) industrial solvent usage. (Appendix 1 of the PEDCo report contains more detailed descriptions of each of these seven areas). Section 112 (NESHAPS) of the Clean Air Act will be the principal vehicle for controlling stationary sources, however, the TSCA or possibly Section 211 of the CAA (fuel additive regulations) may be a more appropriate vehicle for preventing benzene emissions from solvent evaporation and gasoline marketing. Where it is necessary to control only new sources, Section 111 (NSPS) may be an effective vehicle.

2. Issues

Many issues are expected to concern the interpretation of health effects information and the degree to which the health risk supports control of specific sources.

Besides the overall problem of weighing health risks, specific issues are as follows:

- a. Since benzene is a presumptive human carcinogen, can any emissions be permitted?
- b. Do restrictions for industrial plants need to be based on site-specific exposure levels or can they be based on typical plant configurations and population exposures?
- c. Can emissions from all suspect major sources be determined with sufficient precision to provide a realistic assessment of the health risk?
- d. Does EPA or do other Federal agencies have authority to regulate benzene or other air pollutant emissions from mobile transport vehicles?
- e. Is the hazard of benzene from using gasoline as a solvent and in boats, lawnmowers, etc. sufficient to warrant benzene removal irrespective of the service station health risk?
- f. While OSHA or Consumer Product Safety Commission regulations may limit benzene to acceptably low levels, EPA would have no control over their enforcement. Should EPA enact parallel regulations in these areas?
- g. As with most volatile organics (VOC), air pollution controls cause few other air pollutants and little or no water pollution or solid wastes. In many instances, process modifications and stack gas treatment will recover benzene and possibly other VOC. In some cases, benzene will have to be incinerated with or without heat recovery; the impact of resulting nitrogen oxides needs to be evaluated.

- h. Benzene treatment processes may yield organic liquids which can't be reused in the process. While these are potential water pollutants, they often can be further processed for by-product recovery or incinerated without impacting liquid effluents. Where liquid wastes are anticipated, the feasibility of effluent restrictions needs to be investigated.
- i. The greatest economic and energy impacts are likely to be encountered where benzene is released in dilute streams or from large numbers of small sources such as service stations. Energy requirements, costs, and economic impact of control alternatives needs to be assessed in developing regulations.

3. Statutory Authorities

OSHA - Occupational Safety and Health Act
 EPA - Clean Air Act (Section 112)
 CPSC - Consumer Product Safety Act;
 Federal Hazardous Substances Act

4. Principal Actions/Schedule (Tentative)

2/78 - OSHA Promulgates Benzene Regulation
 5/78 - CPSC Proposes a ban of benzene as an intentional ingredient or as a contaminant in consumer products at levels of .1% or greater (gasoline and solvents or reagents for laboratory use are exempt).
 8/78 - Finalize EPA Health/Risk Assessment Documents
 1/79 - EPA Proposes First Set of Benzene Regulation
 Fall '79 - EPA Promulgates First Set of Benzene Regulations

5. Principal Technical Contact

EPA - Richard Johnson 629-5355
 OSHA - Jim Vail (919) 523-7193
 CPSC - Stan Morrow (301) 492-6557
 FDA - Edward Seligman (301) 496-4937

6. Recommendations

- A. Coordinate information on benzene content in solvents and the effectiveness of joint regulatory action with OSHA.
- B. Explore possibility of joint research to develop insights regarding the effects of long-term exposure to low levels of benzene.
- C. Coordinate studies necessary to make regulatory decisions on the control of benzene exposure at service stations:
 - OSHA/EPA - Initiate study of the implication to benzene levels in gasoline line of lead phase down regulations.
 - OSHA/EPA - Initiate study of the health effects of exposure to other toxic organics contained in gasoline.

Beryllium (Be)

1. Background

A. Health Effects

The health effects of inhaling beryllium particulates which have been of primary concern to OSHA and EPA include the acute and chronic forms of beryllium disease and its potential to induce cancer in humans. In addition, EPA is involved in regulation of beryllium content in aquatic environments due to its toxicity to fish and invertebrates.

Beryllium-induced acute respiratory effects range from a mild inflammation of the nasal mucous membranes and larynx to tracheobronchial involvement and severe chemical pneumonitis. Recovery is generally rapid, ranging from 1-6 weeks for mild cases. However, recovery from acute pneumonitis may be prolonged and severe cases may become fatal.

Chronic beryllium disease is characterized by a latency period ranging up to 20 years or more and is a systemic disease, prolonged in duration and commonly progressive in severity despite cessation of exposure. Pulmonary dysfunction and effects such as heart enlargement, leading to cardiac failure; enlargement of the liver and spleen; cyanosis, and the appearance of kidney stones also characterize the chronic disease.

While the acute form of beryllium disease is rarely seen due to industrial control of very high exposures, chronic disease continues to be seen in many segments of the beryllium industry.

The determination by OSHA to treat beryllium as posing a carcinogenic risk to humans was based, primarily, on the data indicating beryllium as being carcinogenic to test animals. While OSHA feels epidemiological studies are valuable in general, the overwhelming legal and ethical considerations of not using humans as test subjects to determine the carcinogenic potential of a compound has led to reliance upon animal testing in the laboratory.

Observation of beryllium disease and experimental cancer induction has been reported in numerous published articles. A number of these articles have been referenced in OSHA's proposed beryllium standard (40 FR 48814) and in OSHA's notice of public hearing (42 FR 2901) on that proposed standard.

Be is a potent enzyme poison especially where mg is a co-factor including mitosis. Unlike inorganic Pb, Be continues to be active in sites where it is stored and may have a long latent period before it manifests toxicity. Both of these properties are significant for potential carcinogenesis. Be has produced cancer in the respiratory tract of rats and monkeys following inhalation. Although "epidemiology" has not established carcinogenicity in humans, the incidence in two studies was greater than anticipated. The available data indicate that Be should be suspect as a carcinogen.

B. Production/Use

Beryllium is an extremely light metal possessing many qualities which make it very useful in industry, especially as an alloy. Among other things, it is used in the manufacture of ceramic parts, household appliance circuitry, thermal coatings, switch gear and welding apparatus. It is also used in the aerospace and nuclear industries in the manufacture of inertial guidance systems, rocket motor parts, aircraft brake systems heat shields, etc.

C. History and Current Status

OSHA and EPA are the only agencies presently involved with regulatory actions dealing with beryllium.

OSHA

1. Initial 6(a) adoption from ANSI - 2ug/m³ TWA
5ug/m³ ceiling
25ug/m³ peak
2. Oct 17, 1975 proposed revision - 1ug/m³ ceiling
 - (a) Hearings 8-16 thru 9-12, 1977
 - (b) Final rule due Spring 1978

EPA

1. Dec. 7, 1971 - Proposed emission standard.
2. April 6, 1973 - Final emission standard - 10ug/24 hours³
or 0.01ug/m³ at
emission source averaged over 30 days.
3. Water Quality Criterion published in 1976 limiting beryllium content in aquatic environments is presently being revised - Due July 1978.

2. Issues

There appears to be clear consensus among the concerned Federal agencies that beryllium is a highly toxic substance and exposure to beryllium should be strictly limited. There may be less than total agreement among some staff members as to whether beryllium is a human carcinogen and if so, what level of exposure would protect against cancer induction in humans.

3. Statutory Authority

OSHA - Section 6(b) of the OSH Act of 1970
EPA - FWPCA §311, CAA §112

4. Principal Actions/Schedules (tentative)

1971 - OSHA Occupational Exposure Standard
1973 - EPA Final Emission Standard
10/17/75 - OSHA proposed revision
1976 - EPA Water Criterion Standard
1977 - OSHA Hearings on revision
Summer
1978 - EPA Revision to Water Criterion Standard

5. Agency Technical Contacts

OSHA - Robert Manware 523-7183
EPA - John Carroll 245-3042
Len Guarraia 245-3042

6. Recommendations

EPA and OSHA have developed Agency activity summary sheets which have been received by the appropriate Agency Technical Contacts.

Phone contact has been made between EPA and OSHA IRLG representatives resulting in the following suggestions:

- A. Provide routine mailing of such items as FR publications, relevant correspondence, literature, etc.
- B. Maintain periodic telephone contact regarding anticipated agency activities, provide notice of meetings, seminars, etc. of possible interest.
- C. Provide indices of and access to Agency resources, (including literature and, staff resources) non-governmental contacts, and ongoing research or contracts.
- D. Establish contact with other Agencies such as FDA and CPSC who are not presently regulating beryllium but may in the future and provide those agencies with activity summaries, pertinent literature, etc.

Cadmium (Cd)

1. Background

A. Health Effects

As evidence emerges on the risks of environmental exposure to cadmium, increasing, concern mounts over the accumulation of cadmium in the body at low level exposures. Cadmium, which is used in a variety of commercial and consumer products, is believed to reach man through a number of routes. There is recent concern over the presence of Cd in sludge which might reach the food chain as a result of leaching from disposal sites or its use as a soil conditioner. Cadmium particulate in air falls out into water and soils. Plants take it up from the soil, and people and animals ingest Cd from these sources. Ingestion from contaminated water has not been so well documented.

About five percent of ingested cadmium is absorbed into the body, and its biological half-life in humans is estimated to be on the order of 15 years. Absorbed cadmium accumulates in the kidneys and liver. At kidney cortex levels of about 200 ppm, cadmium may cause damage to the renal tubules. Osteomalacia (bone softening) has been observed at higher exposure levels. Analyses of autopsy tissue samples show current levels of 15 to 50 ppm in the kidney cortex of people over the age of 50 who were not occupationally exposed; the higher levels generally reflect those found in individuals who had been smokers.

Prolonged exposure to cadmium dust can cause emphysema. Some epidemiological studies indicate a relationship between several forms of cancer and occupational exposure to cadmium oxide dust and fumes. Hypertension has been developed in laboratory animals after prolonged exposure to low levels. Studies of Cd in fetal tissues during prenatal life shows that the metal traverses the placenta. Experimental studies in laboratory animals have also shown that Cd is a potent teratogen.

B. Production/Use

Cadmium is produced as a by-product of zinc refining. In 1974, the total U.S. consumption of cadmium was about 6300 metric tons, at a cost of about \$8500 per metric ton. About one-third was imported. By 1985, demand is expected to reach 9600 metric tons. Of the total use in 1975, about 55 percent went to electroplating, 21 percent to plastic stabilization, 12 percent to pigments, 5 percent to batteries, and 7 percent to a variety of other uses. Major growth is expected in the nickel-cadmium battery industry.

The identifiable releases of cadmium to the environment were estimated at a total of 1800 metric tons for 1974. Of this, about 20 percent was from zinc mining and smelting, via air, water, and tailings; fifty percent was from such indirect sources as fossil fuel combustion, fertilizer use, and disposal of sewage sludge; and thirty percent was from industrial

uses, such as remelting of cadmium-plated scrap, incineration of plastics containing Cd, and electroplating.

The major direct sources of human exposure to cadmium are food, tobacco, water, and air contamination. Groundwater contamination as a result of waste disposal is common. FDA's market basket survey has been identifying low levels of Cd in most composite class samples. Thus, virtually everyone is exposed to trace levels of Cd. Recent studies indicate that, in Sweden, Cd concentrations in wheat may be increasing at a rate roughly proportional to levels of industrial use. Current estimates of U.S. dietary levels approximate the provisional tolerable intake of 400 to 500 ug/week recommended by the joint Food and Agriculture Organization of the United Nations and the World Health Organization Expert Committee on Food Additives (FAO/WHO). This allows a safety factor of only about four for intake from non-dietary sources in the U.S.

C. History and Current Status:

1. OSHA has received a criteria document from NIOSH for occupational exposure to cadmium and other heavy metals. Review of the document and preparation of an occupational exposure standard is scheduled to begin in June 1978. OSHA anticipates publication of a proposed standard in December 1978. The Work Group should review the health criteria and sensitive populations used in standard setting by OSHA and other agencies to issue a joint statement explaining major differences in their standard development procedures.

2. CPSC, FDA, and EPA are currently reviewing issues relevant to the use of cadmium pigments in decorative frits on glassware. A public statement is scheduled to be made in January 1978. This activity may provide an example for future cooperative efforts which could be coordinated through the Work Group.

3. EPA, OSHA, FDA, CPSC, NBS, DOD, NIEHS, DOI, AND GSA participated in a year long cooperative effort which, in October 1977, culminated in a jointly sponsored Government-Industry Workshop on Alternatives for Cadmium Electroplating in Metal Finishing. The Workshop reviewed methods for reducing cadmium pollution from electroplating as well as alternatives to cadmium electroplating in specific applications. Panel discussions were held on specifications and standards for cadmium plating and on the essentiality of electrodeposited cadmium. Industrial representatives have requested that future workshops of this nature include steering committee members from industrial and international groups. The EPA and the American Electroplaters Society cosponsored a conference in January 1978 on Pollution Control in Metal Finishing. The Work Group should consider this mode of obtaining information on control technology, alternative materials, and essential uses for other cadmium products.

4. FDA and USDA are jointly sponsoring a study of the effect of sludge on cadmium levels in edible crops. The EPA Office of Solid Waste is working closely with FDA and USDA in developing regulations and guidelines for disposal of cadmium bearing solid wastes on agricultural lands. The Cadmium Work Group may obtain progress reports and may request opportunity for review of cadmium criteria through EPA representatives. However, interagency review is being coordinated by the Work Group on Waste Disposal to Food Chain Land. In the event FDA develops criteria for acceptable levels of cadmium in the total diet or in various foods, the Work Group should coordinate development or modification of solid waste disposal criteria to reflect the acceptable levels in foods determined by FDA.

5. The EPA Office of Pesticide Programs (OPP) has issued Rebuttable Presumption Against Registration (RPAR) of Cadmium Pesticides. This action is based on chronic risk criteria of oncogenicity, mutagenicity, and teratogenicity. Various EPA offices are now seeking interpretation of the assessment of cadmium carcinogenicity in relation to their programs, and the Office of Water Supply is consulting with the National Cancer Institute concerning the potential for a carcinogenicity study in animals via oral administration of cadmium. FDA has also expressed interest in the interpretation of cadmium carcinogenicity data with respect to the Delaney Clause. A focal issue of the Cadmium Work Group should be the implications to the various programs of each agency of the available carcinogenicity, mutagenicity, and teratogenicity data.

6. EPA is currently participating in an international cooperative effort among the U.S.A., Sweden, and Japan to study human populations exposed to cadmium. In addition, the Organization for Economic Cooperation and Development (OECD) maintains several activities relevant to cadmium in the environment. The Work Group should make use of this important source of international research and cooperation.

7. In addition to the activities previously discussed, several projects are underway or being planned within EPA and FDA which are directed toward analysis of environmental and human exposures and, ultimately, criteria development. The FDA Division of Nutrition is conducting research in two areas of interest: The effect of essential dietary elements and food constituents on metabolism and toxicity of cadmium; and metabolism of trace levels of cadmium occurring in foods. FDA annually conducts the Market Basket Survey to establish normal background levels of cadmium in the food supply. Specific foods which contain potentially high levels of cadmium are also monitored. The EPA Office of Water Planning and Standards is revising the water quality

criteria for cadmium. The National Environmental Research Center (EPA, Cincinnati, Ohio) has prepared a document on "The Environmental Impact of Cadmium." The EPA Office of Air and Waste Management in conjunction with ORD and CAG is conducting a health, exposure, and risk analysis of air pollution sources of cadmium and will attempt to determine the contribution from air sources to total cadmium exposure in the general population. The EPA Office of Water Supply is planning a similar study of drinking water exposure and has considered attempting to identify the relative contribution to cadmium exposure from foods. The Office of Toxic Substances is reviewing the environmental and health impacts which may be anticipated from various limitations and control options for cadmium. The Office of Pesticide Programs has conducted an exposure study for cadmium pesticides. CAG will also be reviewing responses to RPAR of cadmium pesticides to evaluate population risks for carcinogenicity and mutagenicity from exposure to cadmium pesticides. The Cadmium Work Group should give immediate priority to the coordination of these exposure analysis activities to provide a unified information base from which standards criteria may be developed and tailored to the needs of each program. The Work Group should also provide for interagency review in order to minimize and reconcile differences which will otherwise occur.

2. Major Issues

A. Issues:

The Cadmium Work Groups should review the following topics for resolution of major interagency issues:

1. Are sufficient data available to determine the need for regulation based on health and environmental effects? Are criteria available to determine safe exposure levels?
2. How are the carcinogenicity, mutagenicity, and teratogenicity data for cadmium to be interpreted regarding the varying legislative mandates? How do we reconcile differences in data interpretation?
3. Are sufficient data available on occurrence (frequency and levels) of cadmium in foods, frequency of population exposure, and health effects in exposed populations for FDA to establish guidelines for cadmium in foods under Section 406 of the Food, Drug and Cosmetic Act? This information and potential FDA guidelines are vital to each of the agencies in assessing contributions to total exposure from various sources and in establishing exposure guidelines and standards for other sources.
4. What level of human intake are currently attributable to exposures through various environmental media including food, air, water, and soil waste? Do these levels separately or in combination represent risks to human health?

5. What measures need to be taken to prevent increased exposures to cadmium in the environment and in the food chain? What are the most appropriate regulatory alternatives for this purpose?

6. How should we address interagency issues concerning cadmium levels in wastes used for agricultural soil amendments?

7. What environmentally safe and economically viable alternatives to the various cadmium uses are available? What are the essential uses of cadmium? What are the safe uses of cadmium in terms of human health and environmental safety?

8. Does cadmium serve any essential biological functions? If so, what levels are required?

B. Major Regulatory Alternatives:

The regulatory alternatives available are:

1. CPSC

- (a) Use of CPSC authority to limit the uses of cadmium through at least two potentially applicable authorities. At the present time, CPSC is actively involved in the investigation of one use and, where overlap exists, has indicated willingness to participate with authorities of other agencies in future coordinated activities concerning cadmium bearing consumer products.

2. OSHA

- (a) Use of OSHA authority to limit occupational exposure and hazards.

3. FDA

- (a) Use of FDA authority to establish guidelines for cadmium in food products, drugs and cosmetic products, if indicated, based on new USDA data on food consumption when such data becomes available.
- (b) Use of FDA authority to establish guidelines for cadmium in chemicals for food uses, i.e., revise specifications for heavy metals in the Food Chemical Code to be specific for elements of concern.

4. EPA

- (a) Use of EPA authority under Section 111 or Section 112 of the Clean Air Act for regulation of air emissions of cadmium.

- (b) Use of EPA authority under the Resource Conservation and Recovery Act to regulate (1) all aspects of handling and disposing of hazardous cadmium-bearing solid wastes and (2) disposal of non-hazardous cadmium-bearing solid wastes.
- (c) Use of EPA authority under the pesticide laws to regulate the use of pesticides containing cadmium and its compounds.
- (d) Use of EPA authority under Section 1412 of the Safe Drinking Water Act to limit levels of cadmium in drinking water.
- (e) Use of EPA authority under Title I of the Marine Protection, Research, and Sanctuary Act to limit ocean dumping of cadmium bearing wastes.
- (f) Use of EPA authority under the Federal Water Pollution Control Act to regulate spills of hazardous cadmium compounds (Sections 311b, 2,A, and 501,a), establish effluent guidelines for various industrial point source categories (Section 307), and provide water quality criteria for protection of aquatic species (Section 304,a).
- (g) Use of EPA authority under Section 6, of the Toxic Substances Control Act to regulate the manufacture, distribution, use, or disposal of cadmium or any of its compounds.

C. Litigation:

No effects on existing litigations are expected. In light of the high level of organization of the cadmium industries, litigation of cadmium regulations may be anticipated.

3. Statutory Authority

CPSC - Federal Hazardous Substances Act; Consumer Product Safety Act.

FDA - Food, Drug and Cosmetic Act.

OSHA - Occupation Safety and Health Act of 1970 (current standards in effect are being revised).

EPA - CAA; RCRA; FIFRA; TSCA; FWPCA; (currently in effect: water quality criteria, effluent guidelines for various industries, and spills regulations); Marine Protection, Research, and Sanctuary Act (Ocean dumping currently limited to trace amounts); Safe Drinking Water Act (current drinking water standard is 0.01 mg/l).

4. Principal Actions/Schedule (Tentative)

9/75	EPA/NERC, Cincinnati - Draft "Environmental Impact of Cadmium"
1/28/77	OSHA - ANPR for occupational exposure
8/77	EPA/CAG - CAG "Assessment of Cadmium"
10/77	EPA/OPP - RPAR decision
12/31/77	EPA/OSW - Propose solid waste disposal facility classification criteria (addresses cadmium in waste disposed to agricultural land)
1/78	EPA/OSW - Sludge Home Use Bulletin
1/78	EPA/FDA/CPSC - Joint statement on cadmium leached from decorated glassware
1/20/78	EPA/OAWM, ORD - Draft air programs Health Effects Assessment and Air Source Assessment
2/15/78	EPA/OSW - Complete municipal sewage sludge disposal intermedia analysis.
Spring, 1978	EPA/OSW - <u>FR</u> notice on Municipal Sludge Strategy
5/5/78	Work Group - Coordinate Cadmium Carcinogenicity policy development.
5/10/78	EPA/CAG, OAWM - Air programs Risk Assessment
5/12/78	EPA/OAWM - Submit air programs package to SAB
Summer, 1978	EPA/OSW - Solid Waste Disposal Regulations
6/73	EPA/OPP - EPA Administrator's decision on RPAR of cadmium pesticides
6/78	OSHA - Begin review of criteria for occupational exposure
7/1/78	EPA/OAWM - Complete EPA Steering Committee review of air programs findings
7/24/78	EPA/OAWM - Submit air programs findings to EPA Assistant Administrators for concurrence

8/15/78 EPA/QAWM - Transmittal of air program findings to EPA
 8/29/78 EPA/QAWM - Decision memorandum on air programs
 10/8/78 EPA/QAWM - FR notice announcing air programs decision
 10/78 EPA/OSW - Landspreading Guidelines
 Fall, 1978 EPA/OSW - Hazardous Waste Regulations
 Fall, 1978 EPA/OPP - Risk/Benefit decision on cadmium pesticides
 12/78 OSHA - FR notice on proposed occupational exposure standards
 5/79 EPA/OTS - Complete analysis of environmental and health impacts of alternative limitations on cadmium
 Annual FDA - Market Basket Survey

5. Agency Technical Contacts

A. Principal Contacts in the IRLG Cadmium Work Group:

Primary responsibility for interagency cooperation on cadmium should reside in the IRLG Cadmium Work Group. Participation of other Federal Agencies should be arranged on specific issues as needed. Coordination issues which need to be resolved are listed in the preceeding section on Major Issues. A schedule for resolution of these issues needs to be developed. The principal contacts in each agency on cadmium are the IRLG Cadmium Work Group representatives:

EPA	- Elbert L. Dage	755-4894
	Richard Johnson	8/629-5355
FDA	- Samuel Shibko	472-5706
	Frank Cordle	245-3114
CPSC	- Joseph McLaughlin	492-6485
DOL	- George Ozga	523-7186

Participation in the Work Group from several additional Federal agencies including the following representatives:

DOC	- George Fitch	377-3691
NIOSH	- Keith Jacobson	443-3680
USBCM	- John Lucas	634-1084
DOI	- Calvin Menzie	632-5316
NCI	- John Munn	496-4663

B. Intra-Agency Coordination:

Each Agency representative to the Work Group should be the point of contact for the Work Group for coordination of Intra-Agency activities.

In view of the multitude of cadmium related activities within EPA, an EPA cadmium coordination committee met in November, 1977 and will continue its purposes as necessary to coordinate EPA activities in support of the IRLG Cadmium Work Group through the EPA Office of Toxic Substances representative to the Work Group. The programs represented in the committee include OTS, QAWM, ORD, OPP, OSW, OWPS, OWS, and CAG. The principal contacts in each EPA program for the ad hoc committee are:

OTS	- Elbert Dage	755-6956
QAWM	- Richard Johnson	8/629-5355 (FTS)
OWPS	- John Carroll	755-3042
OSW	- Bob Tonetti	755-9125
CAG	- Robert McGaughy	245-3039
ORD	- Jay Garner	8/629-2266 (FTS)
OPP	- Richard Troast	755-8050
OSW	- Bill Lappenbusch	755-5643

6. Recommendations

The Interagency Work Group will provide means for information exchange and interagency review on major issues of interest to member agencies. The Work Group will address the following priority topics:

- A. Review and informal coordination of the various exposure analyses being conducted within each agency to reduce duplication of effort and data conflicts. Areas of concern include exposures through occupation, foods, air, water, waste disposal, pesticides, and multimedia sources.
- B. Review of waste disposal criteria for cadmium and coordination with FDA activities on guidelines for cadmium in foods.
- C. Review of the implications of cadmium carcinogenicity, teratogenicity, and mutagenicity data for the various programs of each agency.

- D. Review of health and environmental effects data and availability of criteria for the determination of safe exposure levels.
- E. Explanation of interagency differences in standards development.
- F. Review of CPSC/EPA/FDA actions on cadmium frits for decorated glassware to determine the level of Work Group involvement.
- G. Strategy development for obtaining and using data from international sources.
- H. Plans for decision-making on the potential interagency involvement in gathering and assessing data on control technology, alternative materials, and essential or safe uses of cadmium.
- I. Monthly information exchange on agency activities on cadmium.
- J. The IRLG Cadmium Work Group should provide a forum for interagency review and reconciliation of policy statements from individual programs which impact on total cadmium management or cadmium-related policies of each agency.

Appendix I

Chave, S., et.al., "Zinc and Cadmium in Normal Human Embryos and Fetuses"; Archive Environmental Health, 26:237 (1973)

Cadmium and The Environment: Toxicity, Economy, Control; Paris, Environment Directorate, Organization for Economic Cooperation and Development (1975).

Ferm, V.H., "Development Malformations Induced by Cadmium"; Biol. Neonate, 19:101 (1971).

Friberg, Lars, et al., Cadmium in the Environment, 2nd ed.; Cleveland Ohio, CRC Press (1974).

Fulkerson, William, et al., Cadmium: The Dissipated Element; Oak Ridge National Laboratory (report no. ORNL NSF-EPA-21, January 1973).

National Inventory of Sources and Emissions: Cadmium-1968; EPA, Office of Air and Water Programs (report no. APTD-68, February 1970).

Scientific and Technical Assessment Report on Cadmium; EPA, Office of Air and Water Programs (publication no. EPA 600/6-75-003, March 1975).

Summary Characterizations of Selected Chemicals of Near-Term Interest, EPA, Office of Toxic Substances (report no. EPA 560/4-76-004, April 1976).

Technical and Microeconomic Analysis of Cadmium and Its Compounds, EPA, Office of Toxic Substances (report no. EPA 560/3-75-005, June 1975).

Webb, M., "Cadmium"; Br. Med. Bull., 31(3):246-250 (1975).

Chloroform and Chlorinated Solvents
(Trichloroethylene; Perchloroethylene; Methylchloroform)

1. Background

A. Health Effects

The health effects of chloroform and chlorinated solvents include central nervous system and myocardial depressions, liver disfunction, and carcinogenic reactions. These chemicals are widespread and present a health problem in food additives, cosmetics, drinking water, various mechanical operations and air pollution. These chemicals present a possible health hazard in aerosols, paints, paint-removers, lacquer thinners, degreasers and cleaners. Chloroform is also used as a pesticide and grain fumigant.

B. Production/Use

Chloroform - from controlled chlorination of methane; used as a solvent for fats, oils, rubber, alkaloids, waxes, gutta-percha, and resins; as a cleansing and/or degreasing agent; in fire extinguishers, in rubber industry; as an anesthetic.

Methylchloroform - addition of HCl to 1,1-dichloroethylene; metal cleaning and cleaning plastic molds; solvent in aerosols.

Trichloroethylene - passing tetrachloroethane vapor over calcium chloride catalyst at 300; solvent for fats, waxes, resins, oils, rubber, paints, and varnishes; degreasing; dry cleaning; analgesic and anesthetic; disinfectant and detergent for surgical instruments.

Perchloroethylene - catalytic chlorination of acetylene; dry cleaning; degreasing metals; solvent; and anthelmintic.

2. Issues

- A. Scope of chlorinated solvents - should carbon tetrachloride ethylene dichloride, methylene chloride, vinylidene chloride be included in consideration of interagency exchanges?
- B. To what extent do methylene chloride, perchloroethylene and methylchloroform actually pose a health hazard?
- C. What are the jurisdictional boundaries concerning these chemicals, particularly in regard to water, and do they need clarification?
- D. Can the widely varying priorities each Agency has attached to its investigation and regulatory effort on chloroform and chlorinated solvents be resolved so that the most productive interagency action is not inhibited?

3. Regulatory Authority

A. FDA -

Federal Food, Drug and Cosmetic Act

Section 402 - Adulterated food

Section 409(c)(3) - Food Additives, includes the Delaney Clause which states in part, "that no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal..."

B. EPA -

(1) Clean Water Act

Section 311 - Handling of Chemical Spills

(2) Toxic Substances Control Act

Section 6 - Manufacturing, Processing, Distribution, Commerce Use and Disposal

(3) Clean Air Act

Section 109 - National Ambient Air Quality Standards

Section 111 - Standards of Performance for New Sources

Section 112 - National Emission Standards for Hazardous Air

Pollutants, EPA authority to set standards which provide an ample margin of safety in order to protect human health from hazardous air pollutants.

Sections 150-159 - Ozone Protection

C. CPSC

(1) Federal Hazardous Substances Act

Section 2p - Misbranded Hazardous Substances

Section 3a - Regulation Declaring Hazardous Substances

Section 3b - Establishing Variations and Exemptions

(2) Consumer Product Safety Act

Section 7 - Consumer Product Safety Standards

Section 8 - Banned Hazardous Substances

Section 27E - Manufacturer to furnish performance data to CPSC and/or original protective purchasers

D. OSHA

Occupational Safety and Health Act

Section 6(b) - Occupational Safety and Health Standards

Section 6(c)(1) - Emergency Temporary Standard

Section 6(c)(3) - Permanent Standard - OSHA authority to prescribe standards such that no human will suffer material impairment of health during their working time for any substance while in private employment.

4. Proposed Actions/Schedules (Tentative)

A. FDA

Current Status of Regulations:

- a. Chloroform - On April 19, 1976, FDA proposed to amend the food additive regulations for adhesive and polycarbonate resins by deleting "chloroform" from lists of substances contained in these regulations and for substances prohibited from use in human food by listing chloroform therein. EPA has been notified of this proposal. Chloroform is currently regulated for use as a component of certain food-contact articles (food-packaging adhesives and polycarbonate resins). The only other permitted use of chloroform in or on food is the exemption from the requirements for tolerances established by EPA when chloroform is used as a grain fumigant. It was believed at the time of registration that there was no residue, hence no need for tolerances.

FDA was petitioned by the Health Research Group (HRG) of Washington to ban the use of chloroform in all products under FDA's jurisdiction, recall from the market existing stocks and warn consumers and doctors against the use of such products. HRG cited the study conducted by the National Cancer Institute (NCI). FDA concluded that the NCI report and the HRG petition demonstrated that chloroform is a carcinogen in test animals, vis-a-vis the proposed amendments. But the Commissioner concluded that the potential risk to the public health was not sufficient to require removal from the market of food contact articles containing chloroform or the issuance of a public warning against the use of these products.

- b. Chlorinated Solvents - FDA proposals published in the Federal Register of September 27, 1977 would (1) amend the color additive regulations by deleting trichloroethylene from the list of permissible solvents in certain color additives; (2) amend the food additive regulations to delete provisions for use of trichloroethylene in the manufacturing of foods and food contact surfaces; (3) declare that any human or animal drug product containing trichloroethylene is a new drug or new animal drug and deemed to be misbranded; (4) declare that any cosmetic product containing trichloroethylene is deemed to be adulterated; and (5) declare that pet food or animal food containing trichloroethylene is deemed to be adulterated. Perchloroethylene is currently regulated under 21 CFR §175.105 adhesives.

Future Actions - Summer 1978

Methylchloroform (trichloroethane) §310.507 final rule. The document will amend the new drug regulations by adding a provision requiring an approved new drug application to market any aerosol drug products containing trichloroethane and intended to be inhaled either directly or indirectly.

Proposed rule to prohibit use of perchloroethylene (tetrachloroethylene) in human drug products because a study by NCI shows it to be carcinogenic in test animals.

Proposed rule to prohibit use of perchloroethylene (tetrachloroethylene) in adhesives and foamed polystyrene intended for food contact.

Final rule to (1) amend the color additive regulations by deleting trichloroethylene from list of permissible solvents in certain color additives; (2) amend the food additive regulations to delete provisions for use of trichloroethylene in the manufacturing of food and food contact surfaces.

B. EPA

EPA, OSHA, and CPSC are still basically in the assessment stage in regulating these chemicals. At this time, no timetable for future regulatory actions can be provided.

- a. Chloroform - EPA plans to propose a 100 micrograms per liter standard in drinking water for trihalomethanes. Chloroform is also under review for its use as a fumigant. A Rebuttable Presumption Against Registration (RPAR) was issued on chloroform in April 1976. Because the public views were that all grain fumigants should be reviewed as a class, action on the chloroform RPAR was halted for some time. Data are being gathered in preparation for a request for a risk assessment.
- b. Chlorinated Solvents - Trichloroethylene (TCE) is being studied by a number of groups from EPA. The areas involved include Toxic Substance Control, Air Pollution Control, Water Quality, Drinking Water, Pesticide Regulation, and Solid Wastes. TCE is presently controlled as a hydrocarbon under State Implementation Plans. EPA's air program has initiated study for TCE in anticipation of a potential need for regulations. It is among several synthetic organic chemicals that are under review as precursors of photochemical oxidants, and may be subjected to new source standards for producers. In addition, it is one of several volatile organic chemicals that are under review as possibly requiring regulations as hazardous air pollutants. The recent National Academy of Science drinking water study listed TCE among many problem chemicals. Some

type of regulatory action is required in the near future and the EPA is presently considering available policy options. TCE, an active pesticidal ingredient, is among 150 substances that have been referred to the pesticide program's Special Pesticide Review Division (SPRD). SPRD is presently conducting a preliminary assessment of TCE. In the case of hazardous waste materials, the chlorinated solvents are under consideration for regulation.

A Risk Assessment is currently being conducted by EPA's Carcinogen Assessment Group (CAG) for trichloroethylene. The perchloroethylene risk assessment has been completed.

C. OSHA

- a. Chloroform - OSHA has not had the opportunity to fully evaluate the health effects of occupational exposure to chloroform. Its primary resource document has been the NIOSH criteria document on the subject.
- b. Chlorinated Solvents - OSHA has primarily been concerned with the adverse health effects of occupational exposure to chlorinated solvents in such operations as metal degreasing and dry cleaning. OSHA has an outstanding proposal on TCE, published October 20, 1975. This proposal sets an environmental exposure limit of 100 ppm (8 hour average). No date for a final regulation has been set. An advanced notice on perchloroethylene and methylchloroform was published April 16, 1976, which consisted of a call for information.

5. Principal Technical Contacts

EPA - Mary Reece	755-2972
Pat Hilgard	755-2110
Bob Kellam	8/629-5355 (FTS)
Stan Mazaleski	755-6956
Alma Shea	755-8050
Charles Trichillo	472-6820
OSHA - Robert Cluck	523-7075
FDA - Carl Giannetta	472-5690
CPSC - Andrew Ulsamer	492-6485

6. Recommendations

- A. A determination of the proportion of chlorinated solvents in water, air, consumer products, and food should be made.
- B. As the results of on-going contracts and studies come in, more meetings should be held so that regulatory considerations can be a joint effort.

Information exchanged should include data for the preparation of impact statements, studies on substitute chemicals for the chlorinated solvents which are the focus of the work group at this time, detailed report of analytical methods, data on natural background levels, and chemical, physical and metabolic conversions. The work group should also explore the possibility of establishing criteria for a unified assessment of risk and a master list of contacts each Agency has on the relevant chemicals.

- C. More discussion between the agencies should occur on the possibility of regulating chemicals by classes, specifically chlorinated solvents. At a minimum, methylene chloride must be considered with the four original chemicals.
- D. Members of industry or concerned consumer representatives might be invited to some regulatory work group meetings when regulatory matters concerning their industry are held.
- E. The work group should meet periodically to arrange for the exchange of data and planning for defining common needs and apportioning workloads.

Chlorofluorocarbons

1. Background

A. Health Effects

Chlorofluorocarbons may act to indirectly impair human health by depleting the stratospheric ozone layer. Upon release from an aerosol product or other source, these non-reactive compounds diffuse slowly upward into the stratosphere. In the stratosphere, in the presence of ultraviolet (UV) radiation, photochemical decomposition occurs which liberates free chlorine radicals. The chlorine radicals enter into a chain reaction with ozone molecules, resulting in a net depletion of the ozone layer.

The ozone layer helps shield the earth's surface from harmful UV radiation. As the layer is depleted, the earth's surface is bombarded with more UV radiation. Current estimates are that chlorofluorocarbon emissions at the 1975 rate would result in eventual ozone depletion of 11 to 16 percent.

While the effects of ozone depletion are very difficult to quantify, they may be quite serious. The major immediate concern is that increased UV radiation leads to a statistically significant increase in skin cancer. Some negative effects on plants and animals are likely. The effects of released chlorofluorocarbons, which are the least well understood yet potentially the most serious, are those on climate. Climatic impacts, largely of unknown nature and magnitude, could result from (a) stratospheric ozone diminution, (b) stratospheric ozone redistribution (as would result from increased destruction in the upper stratosphere and increased formation in the lower stratosphere with no net diminution), and (c) absorption of infrared radiation reflected from the earth's surface toward space (likely to result in a net increase in global temperatures). It is expected that regional and local changes in climate (temperature, precipitation, cloud cover, etc.) would be much larger than global averages. The resulting consequences on health and the environment in the U.S. and in other parts of the world are unknown, but significant alterations are a likely possibility.

B. Production/Use

The major uses of chlorofluorocarbon compounds are as aerosol propellants, refrigerants, and foam agents. Certain of the chlorofluorocarbons have major uses as solvents, as fire-extinguishing agents, or as intermediates in the production of chlorofluorocarbon resins and plastics.

The largest commercial use of chlorofluorocarbons has been as propellants in aerosol products. Use as refrigerants is the next largest application of chlorofluorocarbons and is the use for which the chlorofluorocarbons were originally commercialized in the 1930s. The chlorofluorocarbons are used for both refrigeration (localized low temperature cooling) and air conditioning (cooling or rather large volumes of environmental air).

Foaming or blowing agents are used in the plastics industry to produce a finished product in a foamed or expanded form. The chlorofluorocarbons were first used in the production of polyurethane foams, where they impart improved thermal insulation properties because of the chlorofluorocarbon trapped in the cells of the finished product (closed-cell foams). Chlorofluorocarbons are also used to form open-cell foams, in which case they are released to the air. Blowing-agent uses of the chlorofluorocarbons are divided approximately equally between closed and open-cell applications.

Other uses of chlorofluorocarbons include cleaning agents, intermediates in the production of chlorofluorocarbon resins, dielectric fluids, heat-transfer fluids, power fluids, cutting fluids, pressurized leak-testing gases, gases in wind tunnels and bubble chambers, food freezing agents, flame retardants, and sterilant gases.

In 1973, worldwide chlorofluorocarbon emissions were estimated to be about 1,730 million pounds. Propellant emissions accounted for about 1,076 million pounds, refrigerants about 460 million pounds, and other uses (solvents, foaming agents, etc.) about 200 million pounds. The United States emissions were approximately half the worldwide total and Europe contributed an additional third to the total.

Aerosol propellants, solvents, and blowing agents (open-cell applications) are considered to be rapid emitters, i.e., there is a short time delay (usually 6 months) between production and release of the material to the atmosphere. Refrigerants and blowing agents for closed-cell foams involve considerably longer time delays between production and release. None of these uses of chlorofluorocarbons result in decomposition, and eventually almost all of that which is produced reaches the atmosphere.

C. Current Status of Regulations

(1) Nonessential Propellant Uses of Chlorofluorocarbons

- a. Final FDA and EPA regulations and CPSC Notice promulgated in the Federal Register on March 17, 1978
- b. Effective dates:
 - October 15, 1978 - Prohibition on the manufacture of chlorofluorocarbons.
 - December 15, 1978 - Prohibition on the processing of chlorofluorocarbons;
 - April 15, 1979 - Prohibition on the initial introduction of finished products containing chlorofluorocarbons into interstate commerce.
- c. Fed. 20, 1978 - CPSC Propellant labelling regulation (16 CFR-1401 issued Aug. 24, 1977)

(2) Nonpropellant Uses

- a. Collecting and collating information to be used to develop regulatory options (see number 4 below).

(3) Existing Scientific Research Programs:

The Biological and Climate Effects Research (BACER) program provides improved knowledge on the biological effects of stratospheric ozone reduction.

The NOAA-coordinated United States Climate Program Plan will provide improved knowledge of man's impact and potential influence on regional and global climate. The NASA research and development program will provide improved knowledge on the processes of stratospheric ozone reduction. The Interagency Research Coordinating Committee, as mandated under Section 153(d)(1) of the Clean Air Act, will provide improved knowledge on research studies existing at appropriate Federal agencies.

- (4) Chlorofluorocarbons are included in the halomethane group in the 65 chemicals in the court mandate on effluent guidelines and related issues under the Federal Water Pollution Control Act (FWPCA). The Work Group data base could be used to negotiate the mandate for FWPCA action on chlorofluorocarbons.

The BACER program will provide improved knowledge on the effects of stratospheric ozone reduction. NASA research and development program will provide improved knowledge on the process of stratospheric ozone reduction.

2. Issues

- A. What authorities do FDA, CPSC, and EPA have to regulate nonaerosol uses of chlorofluorocarbons, and who should do what?
- B. Do fluorocarbons, other than full halogenated chlorofluorocarbons, need to be regulated?
- C. Are sufficient data available to base the regulations on health or environmental effects or both for the nonaerosol uses?
- D. What, if any, environmentally safe and economically viable alternatives to nonaerosol chlorofluorocarbon use are available?
- E. What health and environmental benefits result from various degrees of regulation and what do these degrees of regulations cost?
- F. What is the appropriate form of the regulation? Should the regulation be a production restriction, end use restriction, recovery requirement, etc?
- G. What timetable should be used to reduce chlorofluorocarbon emissions?
- H. What is the impact of U.S. regulation on the global problem with and without international regulatory action?

3. Statutory Authorities

Aerosol propellant regulations:

- FDA - Federal Food, Drug, and Cosmetic Act
Sections 301, 402, 409, 501, 505, 507, 512, 601, 701(a)
and National Environmental Policy Act (NEPA)
- CPSC - Deferred to EPA (Toxic Substances Control Act)
(except for labelling under CPSA Section 27(e))
- EPA - Toxic Substances Control Act, Section 6

Nonpropellant regulations (should any be proposed):

- EPA - Clean Air Act Amendments, Sections 150-159--ozone protection;
- FDA - May either defer to EPA under the Clean Air Act or regulate
under the Food, Drug, and Cosmetic Act
- CPSC - May either defer to EPA under the Clean Air Act or regulate
under the Consumer Product Safety Act.

4. Principal Actions/Schedules (Tentative)

- 4/26/77 - International Meeting on Regulatory Chlorofluorocarbons
- 5/10/77 - Start as of Tuesday - Work Group Meetings on Regulation for All
Other Uses
- 5/13/77 - Proposed Regulation for Nonessential Aerosol Uses of F-11 and
F-12 published in the Federal Register and Draft EIS to CEQ
- 10/25- First Public Meeting on Nonaerosol Uses
- 10/27/77
- 2/21- Second Public Meeting on Nonaerosol Uses
- 2/24/78
- 3/17/78 - Promulgate Aerosol Regulation and Continue with Analyses to
Determine if Additional Regulation is Warranted

5. Principal Contacts

EPA - George Wirth	426-9000
Federal Bishop	755-8963
FDA - David Klauder	245-3459
CPSC - Colin Church	492-6731
Arlen Slobodow	492-6647
Dorothy Cantor	492-6744
OSHA - Bob Cluck	523-7076

6. Recommendation

Vigorously pursue ban on non-U.S. chlorofluorocarbons as non-essential aerosol propellants.

1. BackgroundA. Health Effects

Chromates are toxic to fish and invertebrates and toxic in activated sludge. In addition, chromates produce tumors in mammals, are irritants corrosives, and cause skin ulcers and inflammation of the kidney.

B. Production/Use

Chromium (VI) is manufactured from chromite ore obtained primarily from the Republic of South Africa, Southern Rhodesia, and the USSR. Human and environmental exposure occurs from chromate production, and from its use in paint and primer pigments, fungicides, wood preservatives and corrosion inhibitors.

2. Issues

There are no issues of conflict between the agencies. In rulemaking, concerns will inevitably be raised concerning the degree of hazard and feasibility of proposed regulations.

3. Statutory Authorities

OSHA - Section 6(b) of the Occupational Safety and Health Act of 1970
(Procedures for developing health standards)
FDA - Food, Drug and Cosmetic Act
EPA - Section 311 of the Federal Water Pollution Control Act

4. Principal Actions/Schedules (Tentative)

1971 - OSHA Initial Occupational Exposure Standard
1976 - EPA Drinking Water Standard, Water Quality Criterion
(Currently being revised)
1978 - OSHA proposed revision to Occupational Exposure Standard
1978 - EPA BAT revisions

5. Agency Technical Contacts

OSHA - Gerald Weinstein 523-9603
FDA - Gerard L. McCowin 472-5740
EPA - John Carroll 245-3042

6. Recommendations

At present, no agency is highly active in regulating chromates. As rulemakings progress, however, technical contacts should receive mailings of technical and administrative publications, notices, etc. on a routine basis. Regular telephone contact to update meetings, shared indices of literature, contacts, and staff assignments should also be maintained.

Coke Oven Emissions

1. Background

A. Health Effects

The purpose of the proposed regulations being developed is to ameliorate adverse health effects associated with coke oven emissions. Epidemiological studies have implicated these emissions as the cause of lung cancer and other adverse health effects in occupationally exposed persons. In addition, many experimental studies using coal tar derivatives and extracts associated with coke oven emissions have identified them as the cause of adverse health effects. Benzo(a)pyrene (BaP), a widely studied carcinogen, is a common constituent of coke oven emissions that has been identified in the laboratory and the ambient air.

More recent findings of elevated levels of BaP in the vicinity of coke ovens indicate that existing control strategies for coke batteries may not be adequate to protect public health. Data from a special air quality study of a steel complex in Johnstown, Pennsylvania, show the impact of coke ovens on ambient levels of BaP. The average value for the eight sampling sites used in this study was about thirty times higher than comparable "background" values measured at National Air Surveillance Network (NASN) sites. One site, which was 0.6 kilometers downwind of the steel mill, showed an average value of about 120 times the NASN "background" concentration.

B. Production/Use

Coke is the porous cellular residue from the destructive distillation or carbonization of coal. It is used as a fuel and reducing agent in blast furnace operations, and in foundries as a cupola fuel. Of the approximately 60 million tons of coke produced annually in the United States, over 90 percent is used in blast furnaces, about 5 percent in foundry operations, and 2-3 percent in other types of industrial plants. Of the total coke production, slightly over 90 percent is produced by steel industry plants, 8 percent by foundry plants (merchant), and 1 percent by beehive ovens. The value of domestic coke is generally rated at about \$115-120 per ton when purchased.

Two basic processes are utilized in the production of coke, one that recovers vapors and other by-products in the coking process (by-product coke ovens) and one that does not (beehive ovens). No new process is presently considered sufficiently advanced to serve as a replacement for currently utilized coking technology.

The coking process involves many complex reactions which can be analyzed in three basic steps. First, there is a breakdown of coal at temperatures below 700° C to primary products consisting of water, carbon monoxide, carbon dioxide, hydrogen sulfide, and other organic compounds. Second, chemical reactions of the primary products occur as they pass through the hot coke, along the heated oven walls and through the hot free spaces in the oven above 700° C, resulting in the formation of aromatic hydrocarbons and other gases. Third, production of the hard coke occurs by the progressive removal of hydrogen.

Twenty to 35 percent by weight of the initial coal charge is evolved as vapors and gasses and is collected in by-product coke production. Many of these gasses are processed to form benzene, xylene, toluene, and naphtha. The coke which consists of the other 65-80 percent of the product is the end-product which is used as a fuel. However, some of the gasses, for example, aromatic hydrocarbons, hydrogen sulfide, and nitrogen containing compounds, are potentially harmful to human health.

C. Current Status of Coke Oven Regulations

The degree of health risk presented to the public by ambient concentrations of emissions from coke ovens is unknown but a preliminary estimate of 150 excess deaths per year has been provided by EPA's CAG. In keeping with EPA policy, this health/risk assessment is being conducted to allow the Administrator to determine whether risks from coke oven emissions warrant action under Section 112 of the Clean Air Act. This Section addresses hazardous air pollutants which cause or contribute to air pollution which may reasonably be anticipated to result in an increase in mortality or an increase in serious irreversible or incapacitating health effects. A thorough public review will be made of available scientific data used to determine the health risk resulting from exposure to ambient concentrations of coke oven emissions (see milestones).

OSHA promulgated a standard for coke oven emissions on October 22, 1976. EPA was involved in several areas of the standard setting process, including a technical review of the OSHA regulatory package by EPA's Offices of Air Programs, and Research and Development, and Enforcement; providing expert testimony at Public Hearings; and providing technical data and methodologies for analytical techniques.

CPSC and FDA are not directly impacted by activities related to coke oven emissions and, therefore, do not desire to designate official contacts on the development plan. However, both agencies are aware of the status and are maintaining contact through IRLG by periodically reviewing progress of the development plan and the RDWG Chemical List status sheet.

2. Issues

- A. A major issue affecting the regulation of coke oven emission sources and other sources of carcinogen emissions results from the inability to identify thresholds below which risk is eliminated. Thus, decisions on the degree of control which is necessary and appropriate, the source categories which should be controlled, and the scheduling and phasing of regulations are difficult. EPA has begun formulating a policy which will provide guidance on such decisions. This policy will form an important basis for the regulation of coke oven emission sources and will potentially affect the scope, degree, and timing of these regulations.
- B. The health risk assessment has been based on epidemiological data for occupational exposure. It can be argued that extrapolation of this data to concentrations to which the public is exposed is not valid because measurement methodology is different and epidemiological studies are lacking at ambient concentrations.
- C. Since coke oven emissions cannot be measured directly, a surrogate or indicator (e.g., BSO, BaP, or other POM's) must be selected to permit regulatory control. Availability of health data, relationship to the carcinogens, and method of measurement are factors in resolving this question. Selection of the surrogate will be made upon completion of the health assessment.
- D. Relating visible emissions (the expected format for some of the coke oven emission sources) to the surrogate for the carcinogens may only be possible in the sense that if visible emissions are diminished, emissions of the surrogate will be diminished. This problem is further complicated as different techniques to measure visible emissions will be applied to the various sources.
- E. OSHA is concerned that if EPA proceeds with rulemaking before a standard is promulgated, such action may pre-empt OSHA's standard because of the way Section 4(b)(1) of the Occupational Safety and Health Act of 1970 is drafted. EPA's Office of General Counsel has indicated that legally no such occurrence is likely. A memorandum of understanding between OSHA and EPA on this issue might be beneficial.

3. Statutory Authority

- OSHA - Occupational Safety and Health Act of 1970, Section 6(b) and 8(c), 29 CFR 1910
- EPA - Clean Air Act, as amended 1977.

4. Principal Actions/Schedule

A. Agency Activities to Date

EPA has prepared draft material related to population exposed to coke oven emissions, review of literature on health data, risk extrapolation, source sampling, and standards support material for an emission regulation. The health, risk, and population exposure data has been submitted to the Science Advisory Board (SAB) for review and a public meeting is scheduled for May 30 and 31, 1978. The standard support document, preamble and regulations will be reviewed by a working group composed of representatives from OSHA, NIOSH, EPA/Water programs, and other interested program offices and later by the National Air Pollution Technical Advisory Committee.

B. Timing of Future Activities

- 5/30/78 - SAB meeting to review population exposure, health, and risk assessment
- 7/78 - List coke oven emissions under Section 112, if appropriate
- 10/78 - Propose regulations for wet-coal charging and topside leaks
- 9/79 - Propose regulations for door leaks

5. Agency Technical Contacts

EPA - Justice Manning	8/629-5231 (FTS)
OSHA - Bob Cluck	523-7105

6. Recommendations

Continued coordination with OSHA in addition to normal EPA Standards Development Working Group meetings.

Dibromochloropropane

1. Background

A. Health Effects

DBCP is a suspected carcinogen and may induce adverse reproductive effects in men. Long term feeding studies have shown that DBCP produces a significant increase in gastric carcinomas in both sexes of rats and mice and causes mammary cancer in female rats. Exposure to DBCP by plant workers and field applicators has resulted in reduced sperm counts. Feeding studies have produced testicular atrophy in rats, rabbits, and guinea pigs.

B. Production/Use

DBCP, a pesticide, is used primarily on cotton, soybeans, peaches, grapes, pineapples, citrus, peanuts, and vegetables. About 25 million pounds of the soil fumigant were produced in 1975 by the Dow and Shell Oil Companies, the only U.S. manufacturers. DBCP may also be present as a contaminant in dibromopropanol, a flame retardant used in urethane foam and other materials.

C. History and Current Status:

- (1) EPA - The RPAR process is being handled through the Office of Special Pesticide Reviews (OSPR), while Cancellation and Suspension are under the purview of the Office of General Counsel.
- (2) OSHA - The Permanent Standard is under the direction of the Office of General Counsel with assistance from the Office of Health Standards.
- (3) FDA - The Office of Compliance has prepared the enforcement guidelines, while the Office of Technology has provided the field sampling program. FDA completed a survey for DBCP in a total of 564 various foods from 10 states, and reported the findings to EPA on January 19, 1978. Only one of the 564 samples contained detectable DBCP, a trace level in one cucumber sample (too low for quantification).
- (4) Legal proceedings may be conducted in the form of cancellation hearings for EPA. No other legal actions are anticipated.
- (5) Cancer Assessment - The EPA Cancer Assessment Group will estimate the potential risks to applicators from pesticide use and to the U.S. population from consumption of food with DBCP residues.

- (6) EPA's RPAR, Cancellation and Suspension Actions - Public comment has already been invited and received on the risks and benefits of DBCP use through the RPAR notice. Registrants have had an opportunity to request a hearing on the Notice of Intent to suspend, but no one sought such a hearing. An amended Notice of Intent to Cancel, will be published shortly and will allow any adversely affected party to request a hearing.
- (7) OSHA Permanent Standard - Hearings were conducted in December 1977, and the permanent standard was made effective April 15, 1978.
- (8) Federal Participation - EPA, OSHA and FDA are the primary actors, but will notify and involve other agencies as needed.
- (9) OSHA has published a Final EIS. EPA's risk/benefit analysis, published as an Amendment to the Notice of Intent to Cancel, will represent a draft EIS.

2. Issues

- A. Does EPA's proposed cancellation/restriction action give farmers and the public protection that is equivalent to the protection offered by OSHA's standard for pesticide plant workers?
- B. Do EPA and OSHA agree on the protective clothing and respirators recommended by EPA for certified applicators?

3. Statutory Authorities

FIFRA - Section 6--Cancellation/Suspension
Section 3--Rebuttable Presumption

OSHA - Section 6(c)(1)--Emergency Temporary Standard
Section 6(c)(3)--Permanent Standard

FDCA - Section 408--Tolerances
Section 304--Seizure of adulterated food

4. Principal Actions/Schedules (Tentative)

12/16/77	EPA - Development Plan to Administrator
12/13/77	OSHA - Hearing begins
12/77 -	EPA - RPAR Work Group Meetings
1/78	EPA - Hearing begins on a later date set by the ALJ
3/15/78	OSHA - Permanent Standard signed
6/30/78	EPA - Amendment to Notice of Intent to Cancel signed by EPA Administrator
1980	Final Notice of Cancellation/Registration

5. Technical Contacts

EPA - Jeff Kempter 755-8053
OSHA - David Welsh 523-7174
FDA - Paul Cornelliussen 245-1152

Other Interested Persons

NIOSH - Barbara Wolf 442-3843
NIOSH - Eugene Kennedy 8/684-4224 (FTS)
NIOSH - Jeffrey A. Lybarger 684-2732
NIEHS - David Rall 8/629-3201 (FTS)

6. Recommendations

None

Diethylstilbestrol (DES)

1. Background

A. Health Effects

It has been reported that DES, if taken by a pregnant woman increases the risk of carcinoma of the vagina or cervix in the female offspring and urogenital lesions in male offspring.

The adverse effects of DES as a drug for human use are similar to those experienced with other estrogenic substances except for vaginal and cervical lesions in female offspring and urogenital lesions in male offspring prenatally exposed. It is not known at this time whether other estrogens would have similar effects on offspring; no cases are reported with other estrogens so far, but other estrogens were rarely used in the same time frame as DES.

FDA has concluded because of the statistically significant association reported between maternal ingestion of DES during pregnancy and the occurrence of vaginal carcinoma in the offspring, that the use of DES or any of its closely related congeners is contraindicated in pregnancy. It has been estimated that about 1 in 1,000 of the offspring of women who have received DES treatment during pregnancy have developed cancer: "Also, it is not definitely known whether this drug may cause other abnormalities in the fetus."

Additionally, a 1972 study reported the occurrence of endometrial carcinoma after stilbestrol therapy in patients with gonadal dysgenesis who were treated with the drug for long periods of time, i.e., five years or more. FDA concluded that the results of this study were not applicable to a five-day course of DES in normal women. Therefore, in spite of the study, there continues to be no relevant evidence at the present time that a short course of DES in normal women, as would be used in postcoital contraception, would expose a woman to an increased risk of cancer of the endometrium. At the same time, it cannot be said that such a risk definitely does not exist.

A preliminary report of a University of Chicago study indicates that DES taken during pregnancy to prevent miscarriage increased the risk of breast cancer and, to a lesser extent, of cervical and ovarian cancer. HEW Secretary Califano has formed a task force to analyze the data. The task force will recommend whether women exposed to DES during pregnancy should be notified of increased cancer risk and what medical followup to take, if any.

Side effects include gall bladder disease, thromboembolic disorders, nausea, and vomiting, breast tenderness and changes, enlargement of benign fibroid tumors of the uterus, edema, abnormal bleeding, headaches, jaundice, mental depression, and effects on the liver.

DES, which is used by feeders of cattle and sheep as a growth promotant, has been shown to cause a statistically significant increase of cancer in female C3H mice at the lowest levels at which it was tested, i.e., 6.25 parts per billion (ppb).

FDA, in 1963, approved methods for the measurement and identification of DES residues in the edible tissues of food producing animals; the mouse uterine method, which measures total estrogenic activity at 2 ppb, and the so-called "paper chromatography" method, which is incapable of differentiating DES from other estrogens at levels below 10 ppb.

Since publication of the detection methods in 1963, FDA has approved numerous new animal drug applications (NADAs) for the use of DES. In each instance, the agency concluded that, when used in accordance with the conditions of use prescribed in the labeling, DES residues could not be detected in edible tissue by the approved methods, and that the requirements of the law were satisfied. Experience with the use of DES and advances in detection methodology have demonstrated that this conclusion is no longer supportable.

Since their original approval, no data have been submitted by the holders of approved NADA's for DES that cast doubt on the finding the drug causes cancer in test animals. Furthermore, radioactive tracer research studies using ¹⁴C-labeled DES, conducted by the United States Department of Agriculture (USDA), have shown that radioactive residues attributable to the use of DES can result even when the prescribed conditions of use are strictly followed, i.e., withdrawal seven days prior to slaughter for DES in feed or implantation of DES 120 days prior to slaughter.

In the face of these findings, it is clear that the central assumption underlying the previous approvals by FDA of DES for use in animals used for human food, i.e., that no residues would be detected when the drug was used in accordance with the currently approved conditions of use, is no longer valid. The currently approved methods for DES have been shown to be inadequate to detect significant residues. Residues being detected by other methods have not been shown to be safe within the meaning of the Act. This showing was not previously required of the applicants since a common premise of all previous DES approvals was that no residues would occur. Moreover, since no level of DES residues has been proven to be safe within the meaning of the Act, the Commissioner concluded that no new method for the detection of DES can now be approved pursuant to the 1962 exception to the anticancer clause (41 FR 1804, January 12, 1976).

B. Production/Use

DES was initially approved (January 1947) for use in poultry as a caponizing agent. In November of 1954 the oral administration of DES was approved for beef cattle with claims for both increased growth promotion and improved feed efficiency. Subsequently, in December 1955 and October 1959, FDA permitted the marketing of DES pellets for implantation in the ear of beef cattle and sheep, respectively. Since the approval of DES for poultry, FDA has ruled that DES implants can no longer be used in poultry due to the residues of DES found in that species. At present, DES is being administered orally and by implantation to beef cattle and sheep.

As a human drug, DES has been marketed as an orally administered effective and inexpensive non-steroidal synthetic estrogen since 1941.

2. Issues

A. Veterinary Drugs Assessment

DES is currently used by the animal industry as a growth promotant. DES when administered to cattle and sheep increases growth rate and improves feed efficiency. The mechanism of action for these responses is unknown. Other estrogens, both natural and synthetic, as well as non-estrogenic compounds, have been shown to produce the aforementioned responses. Estrodial Benzoate, a synthetic estrogen, implanted in combination with progesterone into steers and in combination with testosterone into heifers has been shown to increase growth rate and improve feed efficiency. Zeranol, a fungal produced estrogen-like substance, is also approved for increased growth promotion and improved feed efficiency in sheep and cattle. Some other products approved for improved growth promotion and/or increased feed efficiency in cattle and/or sheep include Zinc Bacitracin, Chlorotetracycline, erythromycin, and oxytetracycline.

Due to information relating to the carcinogenicity of DES, FDA is presently involved in a hearing to remove DES from the market.

B. Human Drug Assessment

DES is a non-steroidal synthetic estrogen that is effective orally and inexpensive.

A number of unresolved and pending issues remain:

- (1) Whether adverse effect on offspring prenatally exposed to DES is specific to DES or whether it is applicable to estrogens as a class. If a drug class effect, it may have serious implications especially with regard to oral contraceptives.

- (2) The pragmatic effect of DES as a postcoital contraceptive for "emergency" use requires further evaluation in view of the new data available from CDC.
- (3) DES is required to have the same labeling (both physician and patient) as other estrogens and must be in accord with published estrogen labeling guidelines (DES as a postcoital contraceptive has special patient labeling).

C. Occupational Assessment

No OSHA proposed standard for occupational exposure is expected in the near future. Some of OSHA's the major concerns are:

- (1) An increased incidence of gynecomastia in male workers in synthetic estrogen and DES implants.
- (2) The relative severity of DES has not been totally assessed at present; however, the potential severity is great.

D. Additional Research Needs

- (1) It is not known whether the adverse effect on offspring prenatally exposed to DES is specific to DES or whether it is applicable to estrogens as a class. If this is a drug class effect, such an effect may have serious implications especially with regard to oral contraceptives.
- (2) The pragmatic value of DES as a postcoital contraceptive for "emergency" use requires further evaluation in view of the new data available for CDC.
- (3) The effect on workers in manufacture and packaging of DES needs to be determined. This would also be applicable to other estrogens.

3. Statutory Authority

A. Food and Drug Administration

- (1) Animal Drug - Statute (Federal Food, Drug and Cosmetic Act)

The authority for regulating animal drugs is found in Section 512 of the Federal Food, Drug and Cosmetic Act, as amended. In addition to those sections listed below, other sections of this Act may be involved in the regulation of a new animal drug such as DES depending on the circumstances giving rise to the need for such regulation (see Sections 301, 302, and 304).

Part 514 constitutes the primary CFR authority regarding the regulation of new animal drugs.

(2) Human Drug

FDA can regulate DES as a new drug for human use under the following authorities:

Statute (Federal Food, Drug and Cosmetic Act):

\$201(p)	New Drug Definition.
\$501(a)(2)(A)&(B)	Adulterated drug if manufactured under insanitary conditions or if not manufactured in compliance with current good manufacturing practices.
\$502(n)	Prescription drug advertising.
\$503(b)	Prescription drug labeling.
\$505	Investigation and marketing of new drugs.
\$510	Registration of drug manufacturers.
\$704	Inspection of drug manufacturers.
\$801(d)	Export of new drugs.

Regulations—21 CFR:

Part 10	Administrative Practices & Procedures.
Part 12	Formal evidentiary hearings.
Part 201	Labeling.
Part 202	Prescription drug advertising.
Part 207	Registration of drug manufacturers.
Part 211	Current good manufacturing practices for finished pharmaceuticals.
Part 310	New drugs.
\$310.501(b)	DES, as oral postcoital contraceptive, the conditions for marketing, patient labeling, and information.
Part 312	Investigational new drugs.
Part 314	New drug applications.
Part 320	Bioavailability and bioequivalence requirements for drugs.

B. Occupational Safety and Health Administration

Section 6(c)(1)—Emergency Temporary Standard
Section 6(c)(3)—Permanent Standard

4. Principal Actions/Schedules (Tentative)

A. Actions to Date: Food and Drug Administration

DES AS A DRUG FOR HUMAN USE

- (1) 1941, New drug applications for DES approved beginning in 1941. Proof of efficacy for labeled indications not required at that time.
- (2) April 22, 1971, Herbst report on association between use of DES in pregnancy and occurrence of vaginal carcinoma years later in offspring.
- (3) November 10, 1971, Drug Bulletin published alerting all physicians and paramedical personnel regarding Herbst finding. Manufacturers notified that DES must list pregnancy as a contraindication in labeling.
- (4) November 10, 1971, Efficacy classification for DES published in the Federal Register - labeling required to list pregnancy as a contraindication.
- (5) February 26, 1975, Federal Register statement no longer allowing "possibly" and "probably" effective indications.
- (6) DES as a postcoital contraceptive.
 - (a) January 26, 1973, Safety and efficacy for this indication review by Obstetrics and Gynecology Advisory Committee on January 26, 1973. Advisory Committee recommended approval for this indication under specific circumstances and with definite directives for use.
 - (b) September 26, 1973, Federal Register statement proposing change in regulations to require patient labeling for DES for postcoital use. New drug applications (abbreviated applications) would be accepted - would require special packaging and patient labeling.
 - (c) September 26, 1973, Federal Register statement proposing withdrawal of approval for 25 mgm. dosage strength of DES for all new drug applications because of "not shown" safety for use for labeled indications.
 - (d) February 5, 1975, Federal Register statement finalizing proposal for patient labeling for DES as a postcoital contraceptive.

- (e) February 5, 1975, Federal Register statement withdrawing approval for those parts of new drug applications for DES with 25 mgms. dosage strength.
 - (f) February 26, 1975, Federal Register statement requiring labeling for DES new drug applications (other than specific NDA's for postcoital use) to contain statement prominently displayed that drug should not be used as a postcoital contraceptive.
 - (g) September 29, 1976, Labeling for DES - DES is required to have same labeling (both physician and patient) as other estrogens and must be in accord with published estrogen labeling guidelines. (DES as a potential contraceptive has special patient labeling.)
 - (h) January 31, 1978, Abbreviated new drug applications for DES as a postcoital contraceptive currently being reviewed in Division of Generic Drug Monograph (DGDM). DGDM has recently raised question regarding efficacy of DES for this indication based on unpublished article by CDC. FDA's Obstetrics and Gynecology Advisory Committee, at its meeting of January 31, 1978 concluded that the experimental design of the CDC study was adequate to support the conclusions drawn by the investigators of that study, namely, that the use effectiveness in the population studied (rape victims) was low. The Committee recommended, therefore, that DES not be used as a standard approach to all rape victims but, rather, that its use be individualized.
- (7) HEW Secretary Califano established a task force to review data concerning breast cancer and use of DES in preventing miscarriages.

DES AS A CAPOINIZING AGENT AND GROWTH PROMOTANT

- (1) January 30, 1947, DES pellets were approved for use in poultry as a growth promotant. Directions for use called for implanting the pellet under the skin at the base of the skull of poultry, so that any unabsorbed pellet residue would be removed with the head at the time of slaughter.
- (2) November 1954, DES, administered orally, was approved for use in beef cattle after consideration of voluminous efficacy and safety data submitted by Iowa State University and Eli Lilly and Company. The application included tissue-residue data (using the mouse uterine assay) which demonstrated that, under the conditions recommended for use, the beef tissue (liver) was free of DES when treated feed was withdrawn 48 hours prior to slaughter.
- (3) December 1955, DES pellets were approved for use in beef cattle. Directions for use called for implanting the pellet in the ear, the ear was not to be used for food for man or animal. Evidence

submitted showed that this use resulted in no detectable residues in meat of the treated animals.

- (4) October 1959, DES pellets were approved for use in sheep. No residues remained in the mutton. Directions called for implanting in the ear, the ear was not to be used for food.
- (5) December 1959, the Secretary of HEW requested the authorized manufacturers of DES for use in poultry to immediately suspend the sale of DES. The Secretary further requested the poultry industry and the retail food industry to immediately discontinue the sale of treated birds. This was done. Industry action was voluntary. This course of action was taken because of evidence, developed after the original authorization for use of DES in poultry was granted, showed that very small residues of DES were found in poultry. The above requests were not based on any violation of the Federal Food, Drug and Cosmetic Act. Subsequently, FDA issued notices of intent to revoke all of the outstanding new drug applications for the use of DES for implantation of poultry (see DHEW/FDA Fact Sheet, May 8, 1961). All but three of the holders of these applications requested voluntary suspension of their applications. The three requested hearings. The hearings were held and the hearing examiner held that all products involved were unsafe except two and recommended suspension of the other new-drug applications. Exceptions to the examiner's tentative order were considered by the Commissioner of FDA. He issued a final order with findings of fact suspending all the NDAs. On December 15, 1961, FDA entered an order suspending the NDA of the three firms.

One holder of an NDA filed an appeal. During the trial, it was stated that on the basis of animal tests and clinical experience, experts have concluded that DES is carcinogenic to man. Prolonged exposure to small amounts of carcinogenic substances has been shown to be more dangerous than single or short term exposure to the same or larger quantities. There is no known threshold or safe level for DES, either as a cause or stimulator of cancer, and there is no known methodology by which such a level can be established. Based on these facts, the Commissioner determined that the use of DES in poultry resulted in residue in the edible portions and was, therefore, unsafe to the consuming public. The U.S. Court of Appeals affirmed the Commissioner's final order. Bell v. Goodard, 366 F.2d 177 (7th C. 1966).

- (6) October 23, 1971, FDA published a proposal in the Federal Register to increase the withdrawal period of DES prior to slaughter from 48 hours to 7 days. In 1954, new drug applications were permitted to become effective for the marketing of DES for the addition to feed of beef cattle on evidence that showed no detectable DES residues in the meat of the animals when the treated feed was withdrawn 48 hours prior to slaughter

as called for in the directions for use. More recent studies utilizing radioactive tracer elements in the feed showed that the actual time for all feed to be eliminated was between 7 and 10 days. A study showed that radioactive DES fed to animals was not detected in any organ or excretion, including the feces, after 132 hours. All DES was thus shown by these methods to be eliminated not only from the edible portions, but also the inedible portions in about 5-1/2 days.

All labels and labeling for the use of DES in feeds which had required a 48-hour withdrawal period were to be revised as soon as possible to provide the 7-day withdrawal period. The document requested that the revised labeling be placed into effect prior to publication of final action on this proposal and required that all changes must be completed within 30 days of issuance of a final order based on the proposal.

- (7) December 8, 1971, the final regulation was promulgated extending the withdrawal time for orally administered DES from 48 hours to 7 days.
- (8) March 11, 1972, a notice of opportunity for hearing was published in the Federal Register, proposing withdrawal of approval of NADAs covering DES liquid premixes for use in the manufacture of feeds for cattle and sheep. This action was based on an evaluation by the Commissioner of new information with respect to such drugs together with the evidence available to him when the applications were approved. The information established that the drugs, when used in the manufacture of finished feeds resulted in contamination of feeds not intended to contain DES.
- (9) June 21, 1972, a Notice of Opportunity for Hearing was published in the Federal Register proposing to withdraw approval of DES NADAs. Due to an increase in reported DES residues the Commissioner of FDA considered whether it was appropriate to withdraw approval of DES, to institute new more effective restrictions to reduce illegal residues, or to take other action. Prior to making a final decision as to the appropriate course of action, additional information was needed from all segments of the public. He concluded that the most appropriate forum for public consideration of this matter was a public hearing and that it would be appropriate to propose withdrawal of the approval for the new animal drug applications for DES in order to utilize the hearing mechanism provided in the statute for this purpose. The Commissioner had not yet concluded that withdrawal of approval for DES is the appropriate course of action.
- (10) August 4, 1972, an order was published in the Federal Register denying hearings and withdrawing approval of DES NADAs for liquid and dry premixes, and deferring ruling on implants.

This order was based on USDA data (July 1972) obtained by using more sensitive methodology which showed DES residues in animal liver even after 7 days withdrawal. This order covered the Notice of Opportunity for Hearing for Liquid Premixes used in the manufacture of feeds for cattle and sheep, published in the Federal Register of March 11, 1972, and the Notice of Opportunity for Hearing of June 21, 1972, regarding both DES Liquid Premixes and Dry Premixes for use in the manufacture of feeds for cattle and sheep and for DES implants for cattle and sheep. This latter notice stated that the earlier notice of opportunity for a hearing with respect to DES liquid premixes would be acted upon at the same time. The notice stated that NADAs for DES liquid and dry premixes were withdrawn, effective immediately.

- (11) December 9, 1972, an order was published in the Federal Register revoking all provisions for use of DES in animal feed. This order revoked all of the regulations providing for the use of DES in animal feed, effective January 1, 1973.
- (12) April 27, 1973, an order was published in the Federal Register denying a hearing and withdrawing approval of NADAs for DES implants. In the Federal Register of August 4, 1972, the Commissioner announced his findings and conclusions with respect to use of DES in liquid and dry premixes, by denying a hearing and withdrawing approval of the NADAs for these uses, and deferred a ruling on use of DES in implants. The ruling on the use of DES in implants was deferred pending receipt of the results of research undertaken by the USDA utilizing radioactive tagged DES implants to determine the absence or presence of detectable residues of DES.

The results of the completed USDA research were transmitted to the Commissioner on April 16, 1973. The data obtained from the USDA radioactive tagged DES implant study clearly established the presence of residues of DES and/or its conjugates 120 days after implantation. Data known or submitted to FDA did not establish any period after which such residues are completely depleted. Thus, it was not possible to set any preslaughter interval following which it could be said with certainty that no residues of the drug were present or would be found.

- (13) May 3, 1973, an order was published in the Federal Register revoking the use of DES implants alone or in combination with testosterone.

- (14) January 24, 1974, the U.S. Court of Appeals handed down its decision holding that the action of FDA in summarily withdrawing approval of the NADAs for DES for use in feed and implants in cattle and sheep was improper. Hess & Clark v. FDA, 495 F.2d 975 (D.C. Cir. 1974)).
- (15) March 27, 1974, a proposal was published in the Federal Register to revoke the presently approved qualitative and quantitative methods for identification of DES residue in edible tissue.
- (16) January 12, 1976, a notice of opportunity for hearing was published in the Federal Register, proposing to withdraw approval of DES NADAs. On the basis of the comments received in response to the proposal to revoke the detection methods for DES, the data cited in the March 1974 proposal, and evidence that DES residues continued to be found in edible tissues of animals slaughtered for human food, the Commissioner concluded that:
- "1. DES has been shown to cause cancer in test animals and has been associated with the occurrence of cancer in humans.
 2. Residues of DES have been and are being detected in the edible tissue of animals at levels that have not been shown to be safe within the meaning of the Act.
 3. The authority conferred by section 512(d)(1)(H) of the Act to approve methods of examination allows, but does not require, the Commissioner to designate a method.
 4. Any method designated by the Commissioner pursuant to section 512(d)(1)(H) must be practicable and capable of detecting drug residues regardless of the route of administration used for a drug.
 5. The approved methods for detection of DES residues in edible tissue are not adequate to demonstrate that, within the meaning of the Act, no residues will be found when the drug is used according to the approved conditions of use.
 6. Data are lacking to justify the approval of any other analytical method(s) for detection of DES residues because no currently available method is capable of detecting residues at levels that have been shown to be safe within the meaning of the Act."

(17) November 26, 1976, the Commissioner published in the Federal Register a final order withdrawing approval of DES NADAs for which requests for hearing had not been received. FDA withdrew approval of the NADAs for use of DES in animals used for human consumption on the ground that use of the drug results in residues that have not been shown to be safe within the meaning of the Federal Food, Drug and Cosmetic Act and that render continued approval of the drug unlawful under the Delaney anticancer clause of the Act, effective December 27, 1976.

(18) November 26, 1976, a notice of hearing was published in the Federal Register on the Commissioner's proposal to withdraw approval of DES NADAs. Four requests for hearing, covering 11 NADAs, had been received and all 4 requests were granted to the extent that a hearing would be held on the continued approvability of those NADAs as to certain issues set out in the notice.

B. Actions to Date: Occupational Safety and Health Administration

DES is the subject of OSHA compliance inspections. There are presently no permanent standards for DES. OSHA cited one DES manufacturer in 1977 for willful and serious violations of health standards, following an inspection which revealed serious employee exposure to DES.

C. Schedules (Tentative)

- 7/31/78 - FDA's Bureau of Veterinary Medicine is presently involved in a hearing to remove DES from the market as a drug used in animals. Initial decision by the Administrative Law Judge by July 31, 1978. Final decision by the Commissioner sometime thereafter.
- 1978 - HEW Task Force to review data of the Chicago study regarding breast cancer and use of DES.
- 9/81 - FDA's Bureau of Veterinary Medicine (BVM) in conjunction with the National Center for Toxicological Research (NCTR) is currently conducting research on the metabolism and carcinogenicity of DES. Also, FDA/BVM is presently involved in developing a radioimmunoassay method for the detection of residues of DES.
- 12/80 - NIOSH is planning a study of the mortality, medical and industrial hygiene problems of workers exposed to synthetic estrogens.
- 4/78 - The National Cancer Institute has an ongoing grant which is funding a screening program of daughters of mother's who have used DES. This screening program which identifies

cases of cervical and vaginal cancers is being conducted at four locations in the U.S.: the Massachusetts General Hospital (Boston, Massachusetts); the Mayo Clinic (Rochester, Minnesota); at Baylor University Medical Center (Houston, Texas); and at the University of Southern California at Los Angeles (Los Angeles, California).

Open - The National Institute of Child Health and Human Development (NICHD) has an ongoing contract with the University of Chicago's Lying-in-Hospital. One of the purposes of this contract is to conduct follow-up examinations with mothers who have used DES. These follow-ups also extend to the children of these mothers. Published data from this study have been reviewed by FDA's Obstetrics and Gynecology Advisory Committee and the data are also the subject of deliberations of HEW's DES Task Force.

1/79 - The National Institute Environmental Health Science is conducting a number of studies on DES in mice. The results of one of these studies, the effects of DES on pregnant mice, will probably be available in January 1979.

5. Principal Technical Contacts

FDA - Richard T. Hunt	443-3480
(Chairman)	
- Ridgely Bennett	443-3490
- Andrew J. Beaulieu	443-1846
- Edison Monk	443-1414
- Fred Degnan	443-4350
OSHA - Patricia Marlow	523-7148

6. Recommendations

A. Possible Joint Actions - Determine if the effects observed for DES are a drug class effect applicable to estrogens as a class.

Ethylene Dibromide (EDB)

1. Background

A. Health Effects

EDB is under review because it has been found to induce oncogenic effects in experimental mammalian species, to induce mutagenic effects, and to produce reproductive effects in experimental animals.

B. Production/Use

The primary use of EDB in this country is as a component in lead-based anti-knock compounds added to gasoline. EDB is also used as a soil and commodity fumigant, as an intermediate in the synthesis of dyes and pharmaceuticals, and as a solvent for resins, gums, and waxes.

C. Current Status of Regulations

(1) OSHA

The current OSHA workplace standard is 20 ppm for an 8-hour weighted average. NIOSH has recommended a reduction of that standard to 0.13 ppm; OSHA is currently reviewing this recommendation and may promulgate this level as the new standard. On November 28, 1977, OSHA issued Guidelines for Control of Occupational Exposure to EDB, which requested employers to limit airborne concentrations of EDB in workers' zones to the lowest possible concentration.

(2) EPA

EDB has been registered for use as a pesticide since the mid-1950's. On December 14, 1977, EPA issued a RPAR of EDB. The basis for the RPAR was experimental evidence that EDB induces oncogenic and mutagenic effects and produces reproductive effects. The Agency is currently reviewing information submitted in rebuttal of the presumption. EPA is also investigating EDB users' sperm count levels and EDB concentrations in the air surrounding fumigation stations.

EDB is also used as a lead-based gasoline additive. As a result of the lead phase-down schedule, the average lead content of gasoline produced by each refinery will be reduced to 0.8 g/gallon of gasoline by January 1, 1978 and to 0.5 g/gallon of gasoline by October, 1979. Thus, if the amount of EDB used in gasoline is directly proportional to the amount of lead in gasoline, the EDB content in gasoline may decrease by as much as 75% between 1977 and 1980.

(3) FDA

FDA is currently analyzing food crops for EDB residues as part of its DBCP effort

2. Issues

- A. What is the hazard associated with the production and use of EDB?
- B. What priority has each Agency attached to its investigation and evaluation of EDB? How can conflicting priorities be reconciled?
- C. What type of coordinated action could be taken by the involved Agencies to reduce the hazards associated with EDB?

3. Statutory Authority

EPA administers a number of Acts which govern the manufacture, processing, distribution, and use of EDB. Among these are FIFRA, the CAA as amended, and TSCA.

OSHA regulates workplace conditions pursuant to the Occupational Safety and Health Act.

FDA, establishes and enforces tolerances and is authorized, pursuant to the Food, Drug and Cosmetic Act, to remove adulterated food from the marketplace.

4. Principal Actions/ Schedules (Tentative)

- 11/2/77 - OSHA issued EDB Guidelines
- 12/14/77 - EPA issued RPAR
- 12/16/77 - EPA Work Plan submitted to IRLG/RDWG
- 1/30/78 - EPA rebuttal comments on RPAR due
- 3/31/78 - EPA rebuttal comments on RPAR due if full extension granted

5. Agency Technical Contacts

EPA - Suzanne Harker	755-5687
OSHA - Flo Ryer	523-7174
FDA - Caesar Roy	245-1186
Support:	
EPA - Dorothy Patton	755-2681
EPA - Irv Auerbach	755-0310
OSHA - Edith Godett	523-7166

6. Recommendations

- A. To ensure coordinated action with respect to EDB, it is essential that EPA, FDA, and OSHA maintain open communication and exchange all relevant information. Such information includes, but is not limited to the following: any air, soil, food or epidemiological monitoring results; exposure estimates of risk assessments; copies of draft or final regulatory actions or proposals; any reports or summaries of Agency's activities or policies with respect to EDB; any information relative to the benefits associated with the use of EDB or to the impact of any regulatory action; and any critical Agency meetings or hearings pertaining to EDB.
- B. Whenever any regulatory action relative to EDB is initiated, the Agency contact should so inform the other Agency contacts.
- C. Agency contacts or their designees are responsible for attending critical meetings or hearings conducted by the other Agencies.
- D. Each designated Agency contact is responsible for obtaining relevant information from other offices in his/her Agency and for forwarding such information to the other Agency contacts.
- E. Each Agency contact is responsible for providing the names of technical, legal, and other support persons.

Ethylene Oxide (ETO) and Its Residues,
Ethylene Chlorohydrin (ETCH) and Ethylene Glycol (ETG)

1. Background

A. Health Effects and Toxicity Review

The following information summarizes some of the toxicity data on ethylene oxide as contained in the EPA's ETO Working Group RPAR, HEW sub-committee report, as well as additional toxicity data received by the ETO Work Group.

(1) Mutagenicity

Available data indicates the mutagenic effects of ethylene oxide in a variety of biological systems include: Drosophila melanogaster, Neurospora crassa, Aspergillus, and a set of Salmonella tester strains. In addition, tests conducted with Salmonella indicate that ethylene oxide induces base-pair substitution mutations. This is consistent with the action of monofunctional alkylating agents. In addition, ethylene oxide has been shown to induce chromosome aberrations in maize, barley, Vici faba, Tradescantia, Drosophila, and rats.

(2) Testicular Atrophy Effect (EPA's Ethylene Oxide: RPAR PD of 1/17/78)

Hollingsworth observed atrophic effects on the testes of eight male guinea pigs which were exposed by inhalation to 357 ppm ETO in 123 seven-hour doses during a 176-day study. All animals survived, but appreciable degeneration of the testicular tubules and replacement fibrosis was noted. Hollingsworth also exposed the same number of guinea pigs to 204 ppm ETO in the same manner and observed a slight decrease in the weight of the testes. However, no histopathological effect was noted. In another test, 20 male rats which were exposed to 204 ppm ETO for 122 to 157 seven-hour periods during 176 to 226 days were noted to have small testes and slight degeneration of tubules. There was no evidence that withdrawal from exposure would allow restoration of the testicular structure. The authors also reported that there was no testicular histopathology or gross effect on guinea pigs or rats that were exposed to 113 ppm ETO in air. The exposure regimen consisted of 122 to 157 seven-hour periods during 176 to 226 days. No measure of fertility was taken in any of these tests.

A study in which male mice were exposed to air contaminated with radio-labeled ETO demonstrated residual radioactivity in the testes. In addition, male rats exposed to ETO in the air demonstrated affected germ cells as evidenced in each of two dominant lethal assays.

(3) Allergenic Response

Sensitization-allergic-type reactions have been reported in workers drenched with ethylene oxide solution and patients exposed to improperly degassed dressings.

In a report of recent skin irritation studies conducted by Shupak, sponsored by the Association for the Advancement of Medical Instrumentation's (AAMI) Ethylene Oxide Sterilization Subcommittee, delayed sensitization in human subjects was observed in response to ethylene oxide contained in polyvinyl chloride blocks and films and in petrolatum. This finding supports an earlier report of anaphylaxis from ethylene oxide residues from ETO used in the sterilization of renal dialysis equipment. Hypersensitivity was referenced in EPA's RPAR.

(4) Human Acute Toxicity

Ethylene oxide is an eye and respiratory tract irritant and a skin vesicant (blistering agent). Nausea, dizziness, and signs of metal disturbance have been observed in humans accidentally exposed to high concentrations of the compound. Signs of acute human toxicity have been reported such as vomiting, ataxia, prostration, labored respiration, and occasional tonic convulsions. Several signs of acute animal toxicity have been reported such as ataxia, prostration, labored respiration, occasional tonic convulsion and death.

(5) Inhalation Acute Toxicity

Inhalation studies show a variable lethal response by species, concentration, and duration of exposure for mice, rats, guinea pigs, cats, dogs, and rabbits. In general, no deaths have been reported at ethylene oxide exposure levels below 150 parts per million (ppm) for these animals. Pathological findings reported on inhalation studies in a variety of species have included growth depression, anemia, posterior paresis, transient paraplegia, and severe lung injury.

(6) Hemolytic Effects

Hemolysis has been reported with ethylene oxide sterilized devices used for blood perfusion in animals and with devices used for intravenous administration in patients.

B. Production/Use (Excerpts from 1977 NIOSH Special Occupational Review and Control Recommendations for the Use of Ethylene Oxide as a Sterilant in Medical Facilities.)

Ethylene oxide (ETO) is a high volume chemical used primarily as an intermediate in the production of ethylene glycol (27% of total consumption), polyethylene terephthalate polyester fiber and film (23%), non-ionic surface-active agents (13%), ethanolamines (9%), with production of di- and tri-ethylene glycol, choline and choline chloride, and other organic chemicals consuming most of the remaining ETO. Although it is estimated that only about 0.02% of the total amount of ETO produced in the U.S. in 1976 was used for sterilization in medical facilities, this amounted to approximately 500,000 kg.

ETO is registered with EPA as a sterilant or fumigant of books, dental, pharmaceutical, medical and scientific equipment and supplies

(glass, metals, plastics, rubber or textiles), drugs, leather, motor oil, paper, soil, bedding for experimental animals, clothing, furs, furniture, and transportation vehicles, such as jet aircraft, buses, and railroad passenger cars.

It has been used also to sterilize or fumigate foodstuffs such as spices, cocoa, flour, dried egg powder, desiccated coconut, dried fruits and dehydrated vegetables and to accelerate the "maturing" of tobacco leaves. At one time, ETO was used briefly as a possible anesthetic agent, but was discarded due to toxic effects.

ETO is manufactured by the catalytic oxidation of ethylene with air (or oxygen) in the presence of silver catalyst. Since 1972, this has been the only method used in the United States. In 1859, ETO was prepared from ethylene chlorohydrin and potassium hydroxide. Until 1957, the chlorohydrin process was the principal method of manufacturing ETO in the United States.

In March 1973, the 13 companies which produced ETO in the U.S. and Puerto Rico had a total production of 1,892 million kg. In 1976, the annual U.S. production of ETO had grown to approximately 2,100 million kg, giving to this chemical a position within the top twenty-five chemicals (by volume) produced in the United States. It is used extensively worldwide. In 1974 production in Japan was 415 million kg. European production in 1972 has been estimated at 865 million kg.

The current U.S. standard (OSHA) for occupational exposure to ETO is 50 parts per million (ppm) parts of air, as a time weighted average (TWA) concentration for an 8-hour exposure, which corresponds approximately to 90 milligrams per cubic meter of air (mg/cu m). The USSR has a standard of 0.5 ppm, (mg/cu m), which was adopted in 1966. Standards of 50 ppm and 20 ppm (36 mg/cu m) are in effect in the Federal Republic of Germany and Sweden, respectively.

There is current large scale industrial use of ETO gas for sterilization of medical supplies and equipment because such use is effective and economical. In addition, alternate methods often are impractical, hazardous, undependable, or uneconomical. Gaseous ETO is generally used industrially for sterilization processing of disposable sterile kits containing items such as disposable syringes and needles, disposable microbiological laboratory supplies, and life-support items such as electronic cardiac "pacemakers," blood oxygenators, and dialysers. An estimated 80% of all such items are processed by ETO gas sterilization in the United States [CDC, 1977]; many could not be processed, regardless of cost, by any other currently available method [CDC, 1977]. The majority of industrial ETO gas sterilization is performed in less than 50 large (greater than 1,000 cu ft) sterilizers and in approximately the same number of smaller industrial units [HIMA, 1976]...

Of the almost 2.1 billion kg of ETO currently produced annually in the United States [Chemical & Engineering News, 1976], it is estimated that 500,000 kg (0.02% of the total produced) are used for sterilization within medical facilities [NIOSH, 1977]. This use is increasing.

NIOSH (1977) estimates that approximately 75,000 health care workers employed in sterilizer areas are potentially directly exposed to ETO. In addition, an estimated 25,000 others are "casually" exposed due to improper or inadequate venting of sterilizers and aerators, storage or use of improperly or incompletely aerated ETO-sterilized items, the physical arrangement of the sterilization facility or workroom (which necessitates passage in close proximity to a gas sterilizer or aerator), and mishandling or failure of the equipment (such as, leaking sterilizer door seals). Thus, the total number of exposed workers in medical and related facilities is estimated to exceed 100,000.

The principal items processed in such hospital "gas" sterilizers are air-powered surgical instruments, anesthesia supplies and equipment, cardiac catheters, endoscopes and other equipment containing lenses intended to be introduced into the human body, humidifiers and nebulizers, implantable body parts, electronic "pacemakers," ophthalmic instruments, x-ray supplies and related equipment, respiratory therapy supplies and equipment, some medications, reusable supplies, thermometers, and equipment contaminated by use in "isolation rooms" (i.e., containing patients with infections).

ETO is used in sterilizers produced by at least six different manufacturers. In certain small sterilizers it is used full strength, or diluted to a composition of 84% ETO with inert ingredients. In larger sterilizers a non-explosive sterilant mixture is commercially available, either 10% ETO/90% CO₂, trade named Carboxide (TM), or 12% ETO/88% halocarbon. Halocarbon products, such as Refrigerant-12 (or -11), sold under trade names such as Freon (TM) or U-con (TM), are used. The Federal standard for occupational exposure to dichlorodifluoromethane (Refrigerant-12) is 1,000 ppm (4,500 mg/cu m) as an 8-hour TWA concentration. No federal exposure limit exists for trichloromonofluoromethane (Refrigerant-11). The impact of the possible removal (for environmental considerations) of certain halocarbon-containing products from general use has not been considered in this report.

C. Current Status of Regulation

1968 -- The U.S. Department of Agriculture Pesticide Regulation Division issued cancellation notices for the registrations of ETO for use on dry beans, all grains, almonds, cashews, chestnuts, filberts, hazelnuts, hickory nuts, pecans, walnuts, and peas. These uses had previously been registered on a "zero tolerance" or "no residue" basis.

1969 -- HEW Commission on Pesticides and Their Relationship to Environmental Health listed ETO as an epoxide compound having chemical structures known to affect DNA. The report stated, "Any compound having such a structure should be proven to be harmless before humans are exposed to it."

1971 -- OSHA adopted the 1968 threshold limit values (TLV's) published by the American Conference of Governmental Industrial Hygienists. This standard limits exposure of ETO in the workplace to 50 ppm or 90 mg per cubic meter of air and was published in 21 CFR 1910.1000 (Table 2-1).

1973 — FDA established an Ethylene Oxide Review Committee to evaluate the hazards associated with the use of ETO.

1973 — FDA published a notice in the Federal Register of September 12, 1973 inviting the submission of published and unpublished data concerning the use, performance, and toxicity of ETO and its reaction products, or any other data having a bearing on the safety and effectiveness of ETO.

1975 — FDA Ethylene Oxide Review Committee recommended publishing interim maximum residue limits for ETO and for its two major reaction products, ETCH and ETG for ophthalmic drugs and topical devices. It recommended and proposed additional toxicity studies.

1977 — EPA established an Ethylene Oxide Working Group. This group's membership is from various offices within EPA. The Chairman is J.B. Boyd, Project Manager, Office of Special Pesticide Reviews. This Working Group has the central responsibility for reviewing and evaluating all information relevant to the continued use of ETO as a fumigant and sterilant by weighing the risks and benefits associated with each use situation. The final result of its efforts will be to provide the Administrator of EPA with regulatory options detailing the trade-offs involved and a recommended course of action. At the present time the following people have been designated as observers of the Working Group proceedings: Boris Osheroff, NIOSH, and Rosa Gryder, FDA.

1977 — HEW Subcommittee on the Benefits and Risks from Use of Ethylene Oxide for Sterilization concluded that ETO was mutagenic. The report further stated that "there is little evidence that it is also carcinogenic to experimental animals, although adequate testing has yet to be conducted."

1977 — The National Institute of Occupational Safety and Health (NIOSH) published Special Occupational Review and Control Recommendations for the Use of Ethylene Oxide as a Sterilant in Medical Facilities. In the preface of this review, it is stated that this type of review is "... prepared in such a way as to assist in the formulation of regulations."

1/27/78 — EPA's Federal Register publication of a "Notice of Rebuttable Presumption Against Registration" of ETO.

1/27/78 — FDA's Federal Register publication of a notice of intent to propose "interim maximum residue limits" and "interim permissible daily levels of exposure" for ethylene oxide, ethylene chlorohydrin, and ethylene glycol.

5/15/78 — EPA's RPAR rebuttal period ended.

2. Issues

- A. Equally safe practical substitutes for the ethylene oxide sterilization of some life sustaining and life saving products such as implanted medical devices, kidney machines and sterile disposables are not presently known. All pesticidal uses of ethylene oxide involve risk/benefit decisions which should be assessed jointly by the IRLG agencies.

- B. EPA is now evaluating the continued uses of ETO as a fumigant and sterilant. Decisions will be based on the risks and benefits of each specific use situation as required by law. Each specific use involves particular concerns. FDA and CPSC may be assessing some facets according to the authorities outlined below. Development of this information along with OSHA's general review of the occupational exposure situation will result in a more informed decision on the continued uses of ETO as a fumigant and sterilant and provide a basis for future regulatory actions involving ETO.

3. Statutory Authorities

A. EPA - TSCA, FIFRA:

(1) Regulations

Section 162.11(a)(3)(ii)(B) provides that a rebuttable presumption shall arise if a pesticide "produces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety."

(2) Pesticide Assessment (From EPA's RPAR of Ethylene Oxide 1/17/78)

There are 38 federally registered pesticide products containing ETO as an active ingredient. One federally registered product contains ETO as an inert ingredient, and there is one application for Federal registration of a state-registered product containing ETO as an active ingredient. ETO is used for sterilization of medical supplies and equipment (on which FDA establishes tolerances) and as an insecticidal, fungicidal, and bactericidal fumigant on copra, black walnuts, and spices. There are EPA-established tolerances of 50 ppm on these stored food products. In addition, ETO is used to disinfect commercial premises, dental instruments, clothing, laboratory animal bedding, laboratory equipment, and pharmaceutical equipment and materials. A more comprehensive site/pest listing has recently been prepared for EPA.

In accordance with Section 24(c) of FIFRA, three ETO products have been registered in states that have demonstrated that these products are necessary to meet special local needs.

(3) Mutagenic Effects (Excerpt from EPA's RPAR of Ethylene Oxide 1/17/78)

"40 CFR Section 162.11(a)(3)(ii)(A) states that "a rebuttable presumption shall arise if a pesticide's ingredient(s), metabolite(s), or degradation product(s) induces mutagenic effects, as determined by multitest evidence." Section 162.3(y) defines mutagenic as "the property of a substance or mixture of substances to induce changes in the genetic complement of either somatic or germinal tissue in subsequent generations." Section 162.3 (1) defines degradation product as "a

substance resulting from the transformation of a pesticide by physicochemical, or biochemical means."

Evidence in both prokaryotic (e.g., bacterial) and eukaryotic (e.g., animal and higher plant) systems indicates that ETO is a general point (gene) mutagen. This means that ETO can interact with DNA of various species to produce mutations in both reproductive and other body cells. There is also evidence that ETO can induce chromosomal mutations in somatic cells of humans and other mammals. In addition, ETCH, an ETO degradation product, has been shown to be a point (gene) mutagen in bacterial systems.

Human exposure to a mutagen has serious implications. The possible adverse effects to people, especially those of reproductive age, are spontaneous abortions, stillbirths, birth defects in their children, and diseases in the adult life of subsequent generations. Any of these effects could result from exposure of either the male or female parent to a mutagen. In addition, those exposed can be adversely affected by mutations of the somatic cells."

The EPA Ethylene Oxide Working Group has concluded that ETO and ETCH meet the risk criterion and are capable of inducing chromosomal mutations in animals.

(4) Reproductive Effects of Ethylene Oxide (Excerpt from EPA's RPAR of Ethylene Oxide 1/17/78)

"40 CFR 162.11(a)(3)(ii)(B) provides that a rebuttable presumption shall arise if a pesticide 'produces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety.' Studies conducted with guinea pigs and rats indicate that ETO can adversely affect the male reproductive organs.

A study in which male mice were exposed to air contaminated with radio-labeled ETO demonstrated residual radioactivity in the testes. In addition, male rats exposed to ETO in the air demonstrated affected germ cells as evidenced in each of two dominant lethal assays.

Hollingsworth et al observed atrophic effects on the testes of eight male guinea pigs which were exposed by inhalation to 357 ppm ETO in 123 seven-hour doses during a 176-day study. All animals survived, but appreciable degeneration of the testicular tubules and replacement fibrosis was noted. Hollingsworth also exposed the same number of guinea pigs to 204 ppm ETO in the same manner and observed a slight decrease in the weight of the testes. However, no histopathological effect was noted. In another test, 20 male rats which were exposed to 204 ppm ETO for 122 to 157 seven-hour periods during 176 to 226 days were noted to have small testes and slight degeneration of tubules. There was not evidence that withdrawal from exposure would allow restoration of the testicular structure. The authors also reported that there was no testicular histopathology or gross effect on guinea

pigs or rats that were exposed to 113 ppm ETO in air. The exposure regimen consisted of 122 to 157 seven-hour periods during 176 to 226 days. No measure of fertility was taken in any of these tests.

In view of these findings, the Working Group has used 113 ppm as the no-observable-effect level (NEL) in assessing the margin of safety for humans.

In the only available epidemiological study mentioning the effects of ETO on the genital system, Joyner examined 37 workers with an average of 10.7 years of continuous occupational exposure to 5 to 10 ppm ETO in the air. There were no statistically greater incidences of such genital disorders as benign prostatic hypertrophy, acute prostatitis, spermatoceles, or seminomas of the testicle. However, no measure of reproductive capacity was taken.

There appear to be two populations at risk with respect to this potential adverse effect: (1) men who use this pesticide in the operation of ETO sterilization equipment on a routine basis and/or spend most of their time in the immediate area of the operation of this equipment, and (2) men who use ETO as a fumigant on a routine basis and/or often enter storage chambers shortly after such fumigation.

The most applicable level of inhalation exposure which is available for sterilization uses is commonly referred to as "a time-weighted average" (TWA). The most accurate indication of exposure to the ETO sterilization user is a TWA taken by continuously monitoring the breathing zone of the user throughout a typical work day and averaging the results. The EPA ETO Working Group is aware that, in practice, ETO sterilization equipment and conditions are many and varied. However, the EPA ETO Working Group has only four TWA's on which to base its exposure estimate. Three of the TWA's were provided by the U.S. Army's Environmental Hygiene Agency and represented the "worst case" for individuals operating the machines tested. These TWA's, 16, 8, and 5 ppm, were well below the 50 ppm standard set by the Occupational Safety and Health Administration and currently in force for the workplace. The fourth TWA was supplied to EPA by a pesticide registrant. The breathing zone was continuously sampled to reflect actual use conditions. The TWA for this sterilization equipment was shown to be 0.16 ppm. The average of the four TWA's is approximately 7.3 ppm.

Assuming 7.3 ppm to be an approximate indication of the amount of ETO to which men using ETO sterilization equipment are continuously exposed, the EPA's ETO Working Group compared this level to the NEL relative to the reproductive effect only in male rats and guinea pigs (113 ppm).

In order to express these exposure levels as absorbed dose levels, compare these doses, and estimate the margin of safety, the EPA ETO Working Group made certain assumptions: (1) rodents and man receive this dose of ETO primarily by inhalation, (2) the efficiency of uptake of the ETO by this route is the same in man as it is in rodents, and (3) the dose is proportional to the respired volume of ETO-contaminated air.

Once the relationship between exposure levels and absorbed dose levels is empirically established for a laboratory rodent, it can be extrapolated to other laboratory rodents and humans. A series of experiments published by Ehrenberg et al. provides the empirical data to determine the dose-exposure relationship for mice. In these experiments the ETO exposure level and duration of exposure varied. There were a total of seven values of exposure (ppm x hour) and absorbed dose during exposure (u mole/kg). These data were plotted and the slope was used to estimate the dose per unit of exposure times the duration of exposure in mice. The Working Group estimated that exposure to 1 ppm for a period of 1 hour gives mice an absorbed dose of 2.8 u mole/kg. Although part of this dose may have been absorbed dermally, the Working Group assumed that most of the dose was absorbed by inhalation.

Using average body weights and respiratory rates, the Working Group estimated average respiratory intake to be as follows:

Humans (68.5 kg males) doing light work:	25.0 liter/hour/kg
Guinea pigs (466 g):	20.6 liter/hour/kg
Rats (113 g):	38.4 liter/hour/kg
Mice (20 g):	72.1 liter/hour/kg

EPA's ETO Working Group then calculated the average daily doses based on the proportion of respired air of guinea pigs, rats, and men to the respired air of mice. The average daily doses administered to the guinea pigs and rats in the Hollingsworth study at the NEL (113 ppm) were estimated to be 28.2 and 52.6 mg/kg, respectively, whereas the daily dose to men doing light work while breathing air containing 7.3 ppm ETO was estimated to be 2.5 mg/kg. The difference between these estimated NEL doses in guinea pigs and rats and the estimated dose for men does not appear to provide an adequate margin of safety.

EPA's ETO Working Group is not aware of any data which quantify exposure to users of ETO fumigants. Labels of ETO fumigation products typically provide that fumigation be done only by experienced operators and that gas masks be worn prior to entering an area that is known to contain ETO vapors. However, the labels indicate that safe entry following fumigation does not require a gas mask unless there is a noticeable odor.

In the opinion of EPA's ETO Working Group, the warning based on noticeable odor is not sufficient to ensure that exposure to potentially hazardous levels of ETO will not occur. Based on published data, the median concentration of ETO which people can detect by smell is 700 ppm; the 95% confidence interval is 317 to 1540 ppm. The presence of other odorous ingredients in these pesticide products complicates precise utilization of these data. Sexton's review of medical and toxicological literature on ETO also treats this issue. He stated that, "When highly diluted with air ethylene oxide is only slightly disagreeable and is readily respirable. Prolonged exposure of this type is associated with early olfactory fatigue, and exposure may be prolonged to the point of considered total absorption of ethylene oxide without warning."

Therefore, entry (e.g., loading and unloading) into the fumigation chambers and vaults between actual fumigation treatments may result in significant inhalation exposure to fumigators. Although EPA's ETO Working Group is unable to quantify the amount of exposure, it is reasonable to anticipate that such exposure is too high in relation to the no-effect levels for reproductive effect only in rats and guinea pigs. Accordingly, a rebuttable presumption against registration has arisen against all pesticide products containing ETO.

EPA's ETO Working Group has also determined that dietary intake of stored food products (i.e., spices, copra, and black walnut meats) which have been fumigated with ETO does not appear to result in exposure to levels of ETO that might affect the gonads. An estimate of ETO ingestion that was based on actual ETO residue data was recently completed. Based on this analysis, EPA's ETO Working Group estimated that a 65-kg man would ingest approximately 0.0003 mg/kg/day. The Working Group concluded that there is an adequate margin of safety between the amount of ETO that might be ingested in stored food products and the estimated doses for which the Working Group has calculated that there will be no effect of testicular atrophic damage (28.2 and 52.6 mg/kg/day in guinea pigs and rats, respectively).

(5) Other Possible Chronic or Delayed Adverse Effects

ETO and its two principal degradation products, ETCH and ETG, have been implicated by several studies as causing certain other chronic effects. The EPA's ETO Working Group is aware that studies currently underway address some of these effects. However, the EPA's Working Group is seeking any and all information which might be available to aid the Agency in further assessment of these effects."

B. FDA - Food, Drug and Cosmetic Act

(1) Human Drugs

The basic regulatory authority for adulterated drugs is Section 501 of the Federal Food, Drug and Cosmetic Act (FDCA). This section of the Act prohibits the addition of a substance not needed in a drug product. Section 505, the new drug section, may also be used to prohibit an unneeded substance. Depending upon the precise circumstances, either or both sections can be used to prohibit the use of a specific ingredient.

(2) Biologicals

Public Health Service Act (PHSA), Section 351
Federal Food, Drug and Cosmetic Act, Section 502(a)

(3) Medical Devices

Federal Food, Drug and Cosmetic Act
Regulations, 21 CFR:
Part 211
Part 821—Medical Devices

(4) Human Drugs, Veterinary Drugs, Biologicals, and Medical Devices Assessment

FDA recognizes that the current use of ethylene oxide as a sterilant for many drug products, medical devices, and other articles is at present necessary for the delivery of required health care.

Ethylene oxide has been used for a number of years as a sterilant for human drugs (e.g., certain ophthalmic and parenteral drug products), veterinary drugs (e.g., ophthalmic ointments for small animals and certain intramammary infusion products), biological products for human use (e.g., tuberculin test preparations and inactivation of some vaccines), medical devices containing heat sensitive plastic components (e.g., heart pacemakers, kidney dialysis machines and heart lung machines), as well as other devices such as surgical sutures, intraocular lenses and surgical scrub sponges. ETO also has been used as a sterilant for the individual ingredients of drug products and for containers, container closures, and delivery systems of drugs and medical devices. Because some drugs, medical devices, and other articles cannot be sterilized by heat, filtration, radiation or liquid chemical agents without degrading or otherwise damaging them, gaseous sterilization must be used. Practical substitutes, including alternative processes and alternative chemicals, for this use of ethylene oxide have not been found.

Because of the local and systemic toxic effects of ETO and its two major reaction products and the known mutagenic effects of ETO and ETCH, the FDA proposes to establish maximum residue limits for ETO, ETCH, and ETG in drug products, medical devices, and certain other articles taking into consideration the lowest possible limits achievable under current good manufacturing practices (CGMPs). In addition, the FDA proposes to establish maximum daily levels of exposure for ETO, ETCH, and ETG to humans and other animals from the use of drug products. These proposed levels of exposure will be based on available toxicity data.

It is possible to determine daily exposure levels from calculations which can lead to estimates of human genetic risk from exposure to ethylene oxide. Certain such estimates suggest that levels considered safe by traditional toxicological tests (for example, measurements of physiological, biochemical, or pathological changes in the body function) might not be considered adequate to protect the public health when the potential for mutagenicity is considered. Calculations leading to estimates of human genetic risk, however, are based upon various assumptions and tests which are in a relatively early stage of evaluation and validation. As the scientific basis for making risk judgements relative to mutagenicity improves, the FDA will reconsider the proposed daily exposure levels. This may involve a further lowering of these exposure levels.

- C. OSHA - OSHA Act, Section 6(c)(1) - Emergency Temporary Standard
- OSHA Act, Section 6(c)(3) - Permanent Standard

The present standard for ETO contained in 29 CFR 1910.1000 (Table 2-1) was adopted in 1971. The airborne concentration of ETO to which any employee maybe exposed at his or her breathing zone shall not exceed 50 parts per million (ppm) or 90 milligrams per cubic meter of air (90 mg/m^3) determined as a time-weighted average (TWA) exposure over an 8-hour work day, in a 40-hour work week. The Federal standard for occupational exposure to ethylene chlorohydrin is 5 ppm of air as an 8-hour TWA concentration.

D. CPSC - Federal Hazardous Substance Act; Consumer Product Safety Act

No CPSC regulatory action is expected in the near future. The major concern of CPSC is the possible presence of ETO and its residues in consumer household products. CPSC has no specific regulation for ETO in household products at this time, however, such contaminated articles would be subject to the general provisions of the Federal Hazardous Substances Act and the Consumer Product Safety Act.

4. Principal Actions/Schedules (Tentative)

- A. 1/27/78 - EPA's Federal Register publication of a "Notice of Rebuttable Presumption Against Registration" of ETO.

EPA issued a "Notice of Rebuttable Presumption Against Registration" (RPAR) for ethylene oxide, based on mutagenicity and reproductive effects. This was the first step in EPA's regulatory procedures which are designed to fully examine the risks and benefits of ETO as a fumigant and sterilant before making any regulatory decision which would substantially affect existing practices.

40 CFR, Section 162.11(a)(3)(ii)(A) states that "a rebuttable presumption shall arise if a pesticide's ingredient(s), metabolite(s), or degradation product(s) ... induces mutagenic effects, as determined by multi-test evidence." Section 162.3(y) defines mutagenic as "the property of a substance or mixture of substances to induce changes in the genetic complement of either somatic or germinal tissue in subsequent generations." Section 162.3(l) defines degradation product as "a substance resulting from the transformation of a pesticide by physicochemical, or biochemical means."

- B. 1/27/78 - FDA Federal Register publication of a notice of intent to propose "interim maximum residue limits" and "interim permissible daily levels of exposure" for ethylene oxide, ethylene chlorohydrin, and ethylene glycol.

The FDA issued a proposal which would improve restrictions on the continued use of ethylene oxide (ETO) as a sterilant for certain drug products and medical devices by: (1) establishing maximum residue limits for ethylene oxide (ETO) and its two major reaction products, ethylene chlorohydrin (2-chloroethanol) (ETCH) and ethylene glycol (ETG), in drug products for human and veterinary use, including biological products for human use, and medical devices, and (2) establishing maximum daily exposure levels for drug products for ETO and its two major reaction products. Any

residues to ETO and its reaction products remaining in a product would be at an acceptable level of safety to the patient to which the product is administered.

- C. 3/78 - FDA's Federal Register publication of proposed "maximum residue limits" and "maximum daily levels" for ETO, ETCH, and ETG.
- D. 5/78 - EPA's ETO Working Group continuing with its review. First objective is to obtain appropriate rebuttal material and determine whether presumption of risk was rebutted.
- E. Open - OSHA is conducting an assessment to regulate ETO through a generic pesticide standard on a generic standard for the standard completion program (SCP). It is expected that either standard will retain a permissible exposure limit of 90 milligrams ETO per cubic meter of air.

5. Principal Contacts and ETO Liaison Group Members

FDA - Rosa M. Gryder (Chairperson)	443-4490
Robert W. Barnes	443-1177
Charles Kunkumian	443-4330
Carl Bruch	427-7230
EPA - Joe Boyd (Project Manager)	755-5632
OSHA - Flo Ryer	523-7174
Edith Godette	523-7166
CPSC - Francine Schacter	492-6557

Regulations Development Work Group Coordinators:

Ronald J. Wylie	443-3480
Wayne A. Matthews	443-3480

6. Recommendations

- A. The IRLG agencies should continue to coordinate their scientific criteria-setting/rulemaking activities and jointly evaluate the risk/benefit issues involved in restricting or prohibiting the use of ethylene oxide for particular products.
- B. Scientists should collaborate on the toxicity of ETO and the evaluation of data. There should, therefore, be a consistent and uniform approach to assessing risks and other key issues such as toxic dose, assumptions for human exposure limits, extrapolations from animals to levels of human exposure, etc.
- C. Enforcement issues should be resolved (e.g., inspections in hospitals, plants using ETO for sterilization) to make efficient use of inspector time and to avoid overlapping or conflicting regulatory actions.

- D. The ETO Work Group should reevaluate the utility of the ongoing and proposed scientific studies originally recommended by the 1973 FDA Ethylene Oxide Review Committee.
- E. Tier 4 mutagenicity studies on ETO should be initiated using I.P. or I.V. route of administration. A research geneticist at the National Center for Toxicological Research (NCTR), has tentatively agreed to do certain supplemental studies related to mutagenicity testing by the method of heritable translocation.
- F. Certain ETO teratological studies are being conducted at NCTR.
- G. Possible Compatible Areas - Under FIFRA, EPA has the authority to establish tolerances for pesticides in foods. ETO is used as a fumigant on copra, black walnuts, and spices. There are EPA-established tolerances for these stored food products. EPA is coordinating its regulatory actions on ETO as fumigants on foods with the FDA. Both EPA and FDA will continue open communication on any proposed ETO regulations.

FDA has authority to regulate the use of ETO as a sterilant on medical devices, drugs, and biologicals. EPA has primary authority to review the continued use of ETO as a sterilant under the "Pesticide Laws." (EPA is now receiving rebuttals of their presumption.) FDA and EPA, are coordinating assessments of the risks and benefits associated with the regulation of the uses of ETO. Through these joint efforts, the agencies will avoid contradiction and achieve an optimal regulatory solution to the problems posed by ETO's use in medical devices, drugs, biologicals, and foods.

OSHA regulations deal primarily with airborne ETO contamination problems in occupational settings. CPSC's major concern is assessing the use of ETO on consumer household products and in determining whether or not ETO is used on any of these products as a sterilant.

In the event that ETO is determined to pose a substantial workplace risk to the users, EPA and OSHA will most likely require an employer to limit employee exposure to ETO to the lowest level feasible. This would be done in the interim before promulgating standards.

- H. Sharing Expertise and Resources - EPA and FDA have agreed to coordinate any new regulatory initiatives involving ETO since both agencies have certain common regulatory jurisdiction.

The members of the ETO Liaison Work Group have been provided a copy of this development plan and the names of contact points in each agency. In developing this plan, information resources were exchanged as discussed above. In addition, each agency has indicated a willingness to give testimony in hearings and other proceedings before other IRLG

agencies. The members have also agreed to provide IRLG agencies with a list of their agencies' expert witnesses should the need arise.

OSHA has provided the ETO Work Group with a copy of its Draft Standard for ethylene oxide.

Both OSHA and CPSC are interested in following the actions of other agencies, and cooperating with their efforts. OSHA would be interested in supporting joint hearings and strengthening research and data sharing.

Note: Appendix I lists the governmental and industrial groups and committees which have been or are currently concerned with ethylene oxide use and/or mutagenicity risk determination. Appendix II lists currently proposed and ongoing studies.

Groups Concerned with ETO

U.S. Government Agencies

1. DHEW Committee to Coordinate Toxicology and Related Programs, Subcommittee on Environmental Mutagenesis. The Committee is soliciting expert outside opinions on ETO mutagenicity and various approaches to risk analysis and the subject will be discussed at its January 9 meeting.
2. DHEW Committee to Coordinate Toxicology and Related Programs, DHEW Subcommittee on the Benefits and Use of Ethylene Oxide for Sterilization.
3. Environmental Protection Agency
 - a) Antimicrobial Pesticides Committee, Cooperative Extension Service, Burton Davis, University of Georgia, preparing pamphlet, "Apply Pesticides Correctly for Control of Microorganisms."
 - b) Two draft documents: (1) Mutagenicity Testing Requirements Section of the FIFRA, Registration Guidelines for Hazard Evaluation of Humans and Domestic Animals, Office of Pesticide Programs, and (b) Criteria for Evaluating the Mutagenicity of Chemicals.
4. NIOSH Special Occupational Hazard Review and Control Recommendations for the Use of Ethylene Oxide as a Sterilant in Medical Facilities prepared by HEW, CDC, NIOSH, Division of Criteria Documentation and Standards Development.
5. USDA Benefits Assessment Team.

Industry

1. Association for the Advancement of Medical Instrumentation/AAMI, ETO Subcommittee
2. Chemical Industries Institute of Toxicology
3. Health Industries Manufacturers Association
4. National Fire Protection Association Sectional Committee on Gas Sterilization of Medical Instruments and Supplies
5. USDA benefits assessment team

Foreign

1. Canadian Standards Association - Publications — Ethylene Oxide Committee; CSA Standard Z 3141.1, 1977; Ethylene Oxide Sterilization for Hospitals; Effect of Sterilization in Hospitals by Ethylene Oxide Process Z 314.2, 1977.
2. The USSR has a standard of 0.5 ppm (1 mg/cu m), which was adopted in 1966.
3. Standards of 50 ppm and 20 ppm (36 mg/cu m) are in effect in the Federal Republic of Germany and Sweden, respectively.

Proposed and On-Going Studies

The ETO Work Group should reevaluate the utility of the ongoing and proposed scientific studies below originally recommended by the 1973 FDA Ethylene Oxide Review Committee in view of new scientific evidence and data.

General Remarks--Route of Administration

Most of the studies now in progress administer ETO by the inhalation route. The RDWG Ethylene Oxide Working Group recommends oral administration for certain toxicological studies and intravenous administration for others, as well. However, most of the device and drug products, for which ETO is currently used as a sterilant, will deliver the compound parenterally into the blood, skin, mucous membranes, ocular and other tissues. The inhalation studies in progress are important to the ETO Work Group's collective view of whether other testing is necessary for regulatory purposes. As the ETO Work Group progresses in its exchange of ideas and information, data gaps can be identified.

Studies Proposed by the FDA Ethylene Oxide Review Committee1. A Hematologic Study

To determine the mechanism of a reported ETO induced anemia in dogs (Woodward and Woodward, 1971) ETO was administered subcutaneously.

Arrangements to do this study were initiated in December 1975 by R. Gryder, ACS and the study was completed by T. Balaz, B.D. Dogs were given ETO-glucose intravenously or ethylene chlorohydrin for 3-4 weeks. The study failed to confirm the occurrence of the anemia reported in the Woodward study.

2. Teratology Studies

The FDA ETO Review Committee recommended oral administration - 2 rodent species - ethylene oxide, ethylene chlorohydrin and ethylene glycol.

In progress:

- (a) 2-year inhalation studies in rat and mice at Carnegie Mellon. Dr. Shelling at Carnegie Mellon has agreed (Nov.30, 1977, telephone conversation) to furnish ACS with a written report of progress to date. R. Gryder, ACS, was supplied with their protocols in July of 1976. After some delay, rat studies began in April 1977.
- (b) Proposed NIOSH inhalation study at the Cincinnati facility. The Work Group has not yet obtained protocols.

Recommendation:

Teratology studies were recommended by the FDA ETO Review Committee. Consideration was to be given to parenteral rather than oral routes of administration. Dr. Holson of

NCTR was contacted by phone (Gryder, ACS, May 1976) to determine whether studies could be conducted at NCTR. Dr. Holdson felt that this would not be high on their priority list. If studies cannot be done at NCTR, they should be contracted. The possibility of joint support with EPA should be explored.

3. Thirty Day I.V. Toxicology Study

Dogs - 3 dose levels of ethylene oxide, ethylene chlorohydrin and ethylene glycol.

The Woodward study reported some toxic effects, other than anemia, even at the lowest dose of ethylene oxide tested (6 mg/kg - 30 days) S.C. and, therefore a reliable "no effect" level was not firmly established for the dog. This type of study, therefore, should be repeated and include lower doses. The route of administration should be I.V. (The dog is reportedly more sensitive to ETO than other species tested).

Recommendation:

This study should be done in-house, at the SPAL facilities in Beltsville, under the direction of Dr. T. Balaz, of the Bureau of Drugs. If this is not possible, it should be contracted.

4. Metabolism Study

No protocols were developed.

Recommendation:

Protocols should be developed which will address the question of enzymatic detoxifying mechanisms and the kinetics of enzymatic detoxification as well as non-enzymatic conversions. This information will be necessary to estimate dose levels of ETO and its degradation products at specific organs (e.g., gonads) and tissues.

5. Mutagenicity

A substantial variety of genetic effects of ethylene oxide and ethylene chlorohydrin has been reported with test systems utilizing microorganisms, insects, plants and rats. While certain of these studies have been criticized as inadequate, the weight of evidence supports the conclusion that these compounds are mutagens. The FDA ETO Review Committee recommended studies in microorganisms (tier 1); *Drosophila* (tier 2); mouse lymphoma (tier 3); and the heritable translocation test in the mouse (tier 4).

- (a) EPA - Office of Pesticides Programs is considering funding a contract through EPA's Triangle Park facility to perform the heritable translocation test in mice (inhalation route of exposure).

Lead

1. Background

A. Health Effects

The public is exposed to lead from multiple sources, including lead in the air, lead in paint and inks, lead in water systems, lead in pesticides, and lead in food. The typical contribution to population exposure from each source is difficult to quantify.

The toxic effects of lead at high exposure are well documented. Among the first effects noted historically were the severe and sometimes fatal consequences such as colic, palsy, and encephalopathy which followed acute occupational exposure in the mining and smelting industries. Exposure to high concentrations of lead in paints, inks, pesticides, and plumbing have also been implicated in cases of severe poisoning.

Recent widespread increase of lead in the environment as a result of human activities has shifted attention to possible health effects of longer-term, low level exposure characteristics of the general population. Of principal concern are effects on blood forming systems, changes in cellular biochemistry, and possible impacts on neurological development. Children are the most sensitive to these effects. Clinical and epidemiological studies have revealed that lead accumulates in the body throughout life, to a large extent immobilized in bone, but with a significant mobile fraction in the blood and soft tissues. Blood lead concentrations respond predictably to changes in the level of environmental exposure and, as a result, are generally accepted as good indicators of that exposure as well as of the internal dose of lead to which all body tissues are exposed.

Animal studies involving very high doses of lead have implicated lead in tumorigenesis. There is no information linking lead to carcinogenesis in humans.

B. Production and Use

Lead ranks fourth among the non-ferrous metals in tonnage used in the U.S.. Approximately 1.2 million metric tons of lead were used in 1975 with an estimated consumption of 1976 of 1.35 million metric tons. Of the total amount consumed, 21 percent is used in metal products; 6 percent is used in ceramics and pigments; 16 percent is used in gasoline anti-knock additives; 54 percent is used in batteries; and the remaining 3 percent is used in miscellaneous products.

C. Current Status of Regulations

EPA - On December 14, 1977, EPA proposed an ambient air quality standard for lead of 1.5 micrograms per cubic meter ($\mu\text{g}/\text{m}^3$), 30-day average. Promulgation of a final standard is scheduled for June 1978.

Performance standards for lead emissions from lead-acid battery manufacturers are being developed. The standards will specify maximum allowable stack gas concentrations of lead in this industry and will apply, depending on the date of promulgation of the National Ambient Air Quality Standard, to new or new and existing sources of lead emissions. Proposal is tentatively scheduled for June 1978 with promulgation to follow in 90 days.

The National Interim Primary Drinking Water Regulation for lead is 50 micrograms per liter (ug/l). A new regulation for lead is being considered as EPA develops Revised National Primary Drinking Water Regulations.

A water criteria document will be completed by June of 1978 which will recommend a guideline level of lead for ambient waters based on health and welfare consideration of both aquatic and non-aquatic organisms (including man).

Regulation of solid wastes containing lead may be undertaken by EPA under the Resource Conservation and Recovery Act.

Effluent guidelines for lead discharge from 21 industrial categories are being developed during the period 1979-81.

OSHA - On October 3, 1975, OSHA proposed an occupational exposure standard for lead of 100 ug/m³, 8-hour time-weighted average. Promulgation of final standards is anticipated during the first quarter of 1978.

FDA - In 1974, FDA proposed a tolerance of 0.3 ppm lead in evaporated milk; final action is planned during 1979. FDA will complete by July 1978, a comprehensive analysis of the legal, economic, and environmental implications of FDA's available control strategies for reducing lead intake. In September 1978, FDA will issue an advanced notice of proposed rulemaking which will include plans for setting limits on lead levels in individual foods and for specifying regulatory status of lead levels in ceramics, other housewares, and cans. FDA hopes to have final regulations by the fall of 1979.

In coordination with CPSC and EPA through an interagency task force, FDA is evaluating the need for regulation of the lead levels in decorated glassware. A public meeting of the task force to discuss the recommendations of the staff toxicologist and an industrial trade association was held on March 7, 1978.

CPSC - In September 1977, under the Lead-Based Paint Poisoning and Prevention Act, CPSC placed a limit of 0.06 percent lead in paint.

2. Issues

- A. Each of the IRLG agencies has followed a parallel path in estimating safe lead dose and attempting to relate this to lead levels in the

media of their concern. These estimates and exposure models may not always be consistent in terms of research, data use, approach of analysis, judgment, or apportionment of lead dose by various media.

- B. Some of the offices have sponsored survey research, without awareness of similar research funded by other offices.
- C. The programs of the various offices are having a significant combined impact on industrial facilities, the total impact of which is not evaluated by any individual regulatory program. For example, some industrial categories will come under regulation by OSHA air, EPA air, EPA effluent water, and EPA RCRA.

3. Statutory Authority

- EPA
 - Safe Drinking Water Act
 - Federal Water Pollution Control Act
 - Toxic Substances Control Act
 - Clean Air Act as amended 1977
 - Resource Conservation and Recovery Act (RCRA)
 - Federal Insecticide, Fungicide and Rodenticide Act
- FDA - Food Drug and Cosmetic Act
- OSHA - Occupational Safety and Health Act
- CPSC
 - Lead Based Paint Poisoning and Prevention Act
 - Federal Hazardous Substances Act
 - Consumer Product Safety Act

4. Principal Actions/Schedules (Tentative)

A. OSHA Programs:

OSHA will promulgate a workplace air standard for lead, in the first quarter of 1978. The proposed OSHA standard is 100 ug/m³, with a blood lead mean target of 40 ug Pb/dl. OSHA's promulgation follows a two-year period after proposal, and extensive collection of comments and hearing testimony. OSHA has not sponsored research projects but has relied on NIOSH, the scientific literature, and public hearings for data.

B. FDA Programs:

FDA's interest in lead derives from the Food, Drug and Cosmetic Act Sections 402, 406, and 409. FDA is also involved in market basket surveys which report lead levels in food. Under its regulatory authority, FDA can set a tolerance, an action level, or actually ban a food contaminant. A tolerance of 0.3 ppm has been proposed for evaporated milk with final action by Fall of 1979. FDA is considering action on infant foods. The threshold for effects in children used by the FDA air standard is lower than that previously taken by FDA's toxicologists. FDA is reviewing the EPA air standard documents. FDA also has a tolerance for lead in silver hollowware of 0.5 ppm, and ceramics of 0.7 ppm. The FDA regulations appear to be based on World Health Organization (WHO) recommended tolerance levels.

C. CPSC Programs:

Possible CPSC authority for lead regulation derives from the CPSC Act and the Federal Hazardous Substance Act. Most CPSC involvement with lead has been directed to paint. The Lead Based Paint Poisoning and Prevention Act resulted in a limit of 0.5 percent lead in paint. This was modified in September 1977 to 0.06 percent. This limit is based on CPSC's view that an avoidable source of lead should be curtailed, rather than a specific health goal for blood lead level.

D. EPA:

- (1) Air Programs - On December 14, 1977 EPA proposed a national ambient air quality standard of 1.5 ug/m (30 day). This is a goal based on a mean blood lead level in children of 15 ug/Pb dl.
- (2) Water Effluent Guidelines - Under the Water Pollution Control Act, EPA will set effluent guidelines for lead discharge from 21 industrial categories phased over the next three years. These standards are developed on the basis of technology of lead removal from effluent. Control of lead discharge is limited by need to remove suspended solids. EPA has also regulated lead discharge from industrial plants under the permit program. There are not quantitative studies relating discharge rates to possible levels of human exposure.
- (3) Water/Criteria and Standards - Under the Water Pollution Control Act, a criteria document is in final stage of preparation which sets a guideline level of lead concentration of ambient waters. This level is based on human health and aquatic welfare considerations.

The recommended levels for ambient waters are considerably below the EPA drinking water standard, and are not used in determining effluent guidelines. The final water criteria document will be issued in June 1978.

- (4) Drinking Water - EPA's criterion drinking water standard is 50 ug Pb/liter. The National Academy of Sciences recently recommended moving the standard to 25 ug Pb/liter or lower. EPA is now considering the level for the final drinking water standard. The drinking water program is proposing research on typical daily dose of lead and their sources.
- (5) Toxic Substances - OTS has a contract with Battelle for a hazard assessment on lead. The first phase of this contract was a multimedia overview of environmental lead. The second phase, now underway, is to examine possible areas in which TSCA authority could be used to regulate environmental lead. A particular interest is the possibility of using TSCA to

control lead exposure from consumer products which may contaminate food supplies, such as food processing equipment. OTS is concerned about lead shot in ammunition posing a inhalation hazard at firing ranges and is also interested in the possibility of encouraging recycling of lead containing products, such as batteries, to avoid environmental contamination by improper or uncontrolled disposal.

- (6) Solid Waste Management - The Resource Conservation and Recovery Act (RCRA) regulates the treatment, storage and disposal of hazardous wastes. While use of a disposal method which will not result in environmental harm is required, the specific disposal method is for the facility with the waste to choose.

Wastes containing lead yielding extracts containing more than a specified concentration of lead may be declared hazardous. The maximum allowable concentration of lead will be based on a belief that improperly disposed of chemical wastes might become an environmental health problem through leaching or leakage of toxicants to drinking and irrigation water aquifers or life-bearing surface waters. Such hazardous wastes must be disposed of in a safe manner. In waste disposal sites, an air emission limit consistent with the ambient air standard would be required.

EPA's Office of Solid Waste Management is sponsoring a Battelle contract to identify lead levels in various waste streams, and the source and disposition of this lead. The effect of RCRA will be to radically change industrial waste disposal practices, and because of the high cost of environmentally adequate disposal, to stimulate recycling.

RCRA air and water standards for disposal sites will probably change with changes in OSHA and EPA air standards and EPA drinking water standards. In addition, other media programs resulting in extraction of lead will create waste material subject to RCRA, with major cost implication for industry.

5. Agency Technical Contacts

EPA - Stan Coerr	8/629-5355 (FTS)
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OSHA - Pat Marlow	523-7148
FDA - Pete Chichilo	472-5690
CPSC - Warren Porter, Jr.	245-2445

6. Recommendations

- A. Through the IRLG, the four regulatory agencies will endeavor to arrive at a joint position concerning the limits to total lead exposure consistent with a common goal for protection of public health, the relative significance of various routes of lead exposure, and the possible coordination of regulatory efforts. Participation in the IRLG group should be augmented with representatives of EPA/ORD, CDC, and HUD.
- B. The Federal agencies concerned with lead will exchange information on critical research findings in the scientific literature, as well as ongoing or contemplated agency funded research projects relevant to lead regulation.
- C. The four agencies will consider the feasibility of combined assessment of economic impact of multiple regulatory actions on certain industrial categories.
- D. Group discussions and information exchanges are of major value and will continue on a regular basis.

Mercury and Mercury Compounds

1. Background

A. Health Effects

(1) In any consideration of the toxic effects of mercury it is important to distinguish between the various chemical forms.

Aryl and alkoxymercurial compounds are rapidly metabolized and show similar toxicological properties to inorganic mercury, primarily causing damage to the kidney. In contrast alkoxymercurials are slowly metabolized, and are known mainly for their effects on the central nervous system which are irreversible and also have the ability to readily cross the placental barrier and enter breast milk. Chronic exposure to metallic mercury vapor most commonly affects the nervous system, although kidney damage may also occur. The toxicity of the various forms of mercury has been extensively documented in the scientific literature. Detailed toxicity studies with experimental animals have been carried out with the various forms of mercury. Additionally, there is an abundance of clinical information relating to human exposure in industrial situations for the inhalation of metallic mercury vapor, and the dust of mercuric salt, as well as the use of mercury-containing drugs, e.g., diuretics. The number of reported poisonings due to aryl and alkoxymercurial mercury is very limited. Poisoning due to alkylmercurials has resulted from the ingestion of mercury contaminated fish in Japan, and treated wheat intended for planting in Iraq, as well as pork derived from pigs fed mercury treated seed in the U.S. The Japanese and Iraqi episodes which involved several hundred individuals are well documented, and have provided a basis for evaluating dose/response effects. The U.S. episode involved a single family.

Dose Response Relationships (Methylmercury) - Data has been derived from (1) the poisoning episodes in Japan and Iraq, (2) fish-eating populations in Peru and Sweden, and Samoan Fishermen, (3) Studies on the metabolism of trace amounts of radio-labelled methylmercury by human volunteers. Data derived from the Japanese episodes indicated that the lowest blood level of methylmercury associated with toxic symptoms was 200 ppb, and a total intake on methylmercury of about 20 mg. In the Iraqi episode, the onset of toxic symptoms was associated with a total intake of methylmercury in the range of 40-60 mg for a 70 kg man, i.e., blood levels of 400-600 ppb. Thus, there is remarkably close agreement in the effect level in these two populations when one considers the many uncertainties and variabilities in these estimates.

In the case of methylmercury exposure, there is considerable concern about its effect on the developing fetus. In the Japanese poisoning episode, infants showing profound neurological effects were born to mothers who were apparently free of symptoms, suggesting the developing fetus is more sensitive to the effects of methylmercury than the adult. This observation has been confirmed in the Iraqi poisoning episode.

Detailed reports on dose responses to methylmercury have been published by the WHO/FAO (1976) (Expert Committee on Food Additives) WHO Environmental Unit, 1976, as well as by EPA.

For Dose/Relationship - Inorganic mercury (including metallic mercury vapor, and the inorganic mercury salts as dusts), and methylmercury see NIOSH Criteria Documents, and also EPA report Mercury in the Environment, A Toxicological and Epidemiological Appraisal (November 1971), and WHO Environmental Unit Report, 1976.

Assessment of Exposure

Sources of Environmental Exposure

Mercury is present in the lithosphere, hydrosphere, biosphere, and atmosphere of the earth. The following table summarizes other reported environmental sources of mercurials:

	<u>Metallic</u>	<u>Inorganic</u>	<u>Aryl</u>	<u>Alkoxyl</u>	<u>Alkyl</u>
Geological	X	X			
Agricultural			X	X	X
Dental	X				
Electrical Equipment	X				
Chlor-Alkali Plants	X				
Paper and Pulp Slimicides			X		
Plants (Pesticides)			X		
Pharmaceuticals		X		X	
Catalyst (e.g., acetaldehyde plants)					X
Thermometers	X				
Burning of Coal	X	X			
Industrial	X	X	?	?	?
Pharmaceutical		?	X	X	
Food (Fish)		?			X

(2) Regulatory actions have been taken to reduce or eliminate entry of mercury into the environment from industrial and agricultural sources. However, the increased burning of coal at power plants could result in a significant increase of mercury in the environment, since it is known that coal contains low levels of mercury. It is not known what impact this might have on levels of mercury in the food chain.

B. Production/Use

Mercury can occur in a number of chemical forms broadly classified as inorganic and organic mercury. The inorganic form of mercury includes elemental mercury, mercurous and mercuric salts. The organic forms include those compounds in which mercury is linked directly to a carbon atom by a covalent bond. Included in this group are the alkyl mercurials (e.g., methyl and ethyl mercury), aryl mercurials (e.g., phenylmercury), and the alkoxylalkyl mercurials (e.g., methoxyethylmercury).

Major uses for elemental mercury are in electrical apparatus, electrolytic preparation of caustic soda and chlorine, and industrial and control instruments. Other uses are in dental preparations, manufacturing of catalysts and pharmaceutical products mildew-proofing paint and agricultural chemicals (primarily fungicides). Most mercury is used in the metal form.

Among the various inorganic mercury compounds, the mercuric oxides, mercurous and mercuric chlorides and mercuric nitrates have wider industrial application than others. Except for the red oxide which is widely used in making mercury batteries, the other mercury compounds are used either as chemical intermediates, catalysts, or as economic poisons. Phenyl mercurials such as acetate or oleate are used as fungicides or antifouling agents in paint preparations. Mercurials have also been used as a seed dressing.

In veterinary medicine, mercury containing drugs have been used as diuretics, antibacterial and antifungal compounds. They have been largely replaced by non-mercurial compounds.

Mercury containing compounds are used as preservatives in various biological products. Preservatives must be added to biological products because they are filled aseptically and they are good growth media for possible contaminating microorganisms. Thimerosal (sodium ethylmercurithiosalicylate) is the preservative most commonly used in products such as Influenza Virus Vaccine, Diphtheria and Tetanus Toxoids, Pertussis Vaccine and globulins at a label claim concentration of 0.01%. This results in a mercury concentration of 25 ug of mercury per 0.5 ml. The dose for vaccines is 0.5 ml which may be administered intramuscularly or subcutaneously in from 1 to 4 doses depending upon the product. The doses of the various globulin preparations are based on body weight and may reach 20-30 ml. In some individuals this dose may be administered once a month depending upon use, i.e., treatment of initial gamma globulin deficiency or maintenance of gamma globulin levels in the case of persistent deficiency. Adverse effects attributable to mercury have not been noted in such patients.

Phenylmercuric nitrate and phenylmercuric borate are also used as preservatives in a few biological products, but they are used typically at lower concentrations.

Mercurial preservatives have been preferred for biological products because they remain active in the presence of high concentrations of protein and they are effective against all types of vegetative microorganisms. Furthermore, they do not have an adverse effect on the potency of the products. No other preservative can be used in such a wide number of products without an adverse effect on potency.

The use of mercurials as a preservative is also permitted in eye area cosmetics, at a level not to exceed 65 ppm. In addition to their use as a preservative in biological and pharmaceutical products, mercurials may also be the active ingredient in some pharmaceutical products such as Vaginal Contraceptives, Diuretics, and eye ointments.

In the late 1960s there was concern for the extent of environmental contamination with mercury in Scandinavia, the U.S. and Canada. At that time, it was recognized that many bodies of freshwater were contaminated with mercury, primarily as a result of industrial activity (mercury discharges from chlor-alkali plants, and also from paper pulp mills). Action was taken to lessen or remove these sources of pollution. However, it was also noted that many lakes areas remote from industrial sources were contaminated with mercury, as a result of erosion of naturally occurring mercurial containing rocks.

Contamination of these bodies of freshwater with mercury resulted in the accumulation of methylmercury in aquatic species. Fish and other aquatic species can accumulate high levels of methylmercury without any apparent ill effect, and thus fish from contaminated areas present an adverse health effect to man. In addition, long-lived ocean species, e.g., tuna and swordfish, may accumulate high levels of methylmercury from normal sea water.

There is evidence to show that there is a so-called "mercury cycle" in nature in which all forms of mercury are capable of being biologically converted to methylmercury, which can again be converted to a more volatile dimethyl form which could produce a discharge of methylmercury into the atmosphere. Microbiological systems can also degrade organic mercury compounds. Their role in nature is not known. However, it seems likely that a balance is maintained in aquatic systems which favor the synthesis of methylmercury. The role of the atmosphere in global and regional transportation of mercury is not clearly defined.

The methylation of mercury (all forms) in sediments on river and lake bottoms is the process of concern for continuous contamination of aqueous systems and their associated biota.

C. Current Status of Regulations

(1) EPA

a. Federal Water Pollution Control Act - Section 307(a) Water Quality Criteria published by EPA in 1972; revision published in 1976; draft revision mercury criterion published on October 17, 1977.

The current draft revision will be finalized by June 1978.

Section 304(g) - Standard methods for sampling and analysis of mercury in water effluents established October 16, 1973. Available methods for measuring Hg in various environmental media (air, water, soil, biological samples, etc.) are being reviewed.

Section 307(a) - In 1973, EPA listed mercury and its compounds as toxic pollutants and proposed effluent standards for discharges to natural waters. This decision has been subject to litigation, and EPA is now reviewing several point source categories to determine the need for effluent guidelines for mercury under Section 307. Guidelines using the best practicable control technology currently available

(BPT) and the best available technology economically achievable (BAT) have been issued for the chlor-alkali industry (chlorine and Sodium or Potassium Hydroxide Production Subcategory).

Section 311(b)(2)(A) and Section 501(a) - EPA has designated six mercury compounds as hazardous substances when discharged into navigable waters from vessels and onshore or offshore facilities.

(2) FDA

a. Cosmetics - Mercury and mercury compounds are not permitted in cosmetics except as mercurial preservatives in eye-area cosmetics. Mercurial preservatives are permitted in eye-area cosmetics at a level not to exceed 65 parts per million (0.0065 percent). Also, cosmetics may contain as a trace element no more than one part per million (0.0001 percent) mercury, calculated as metal as of January 5, 1973.

b. Fish and Shellfish - On December 6, 1974 FDA established an action level of .5 ppm mercury in fish and shellfish. The guideline has been revised, and FDA will announce an action level of 1.0 ppm mercury in fish and shellfish.

c. Biologicals - No limits for mercury have been published in the regulation for biological products. The Bureau of Biologics has been maintaining a limited control program for mercury in the products for which it is responsible. Products submitted are analyzed for mercury to determine that the mercury content complies with the amounts of mercurial preservative specified in the manufacturer's product license and stated on the label. Individual lots of some products have been rejected when the lot was found to contain mercury significantly in excess of the amount claimed on the label.

On a few occasions the level of mercury in the product has been low and it has been found that mercury has been absorbed into the rubber closure.

(3) OSHA

Present standard for mercury (Section 37.8, 1971) contained in 29 CFR 1910.1000, Table Z-2:

Permissible exposure limit of mercury. The airborne concentration of mercury to which any employee may be exposed at his or her breathing zone shall not exceed 0.1 milligrams per cubic meter of air (0.1 mg/m^3) determined as a time-weighted average (TWA) exposure for up to a 10-hour work day, in a 40-hour work week.

(4) CPSC

CPSC has no specific regulation for household products. However, such articles are subject to the general provisions of the Federal Hazardous Substances Act.

D. General Studies

Manufacturing and Use Data -- Data on the manufacture and use of mercury during 1975 is being compiled for the Organization for Economic Cooperation and Development (OECD). Abstracts off that body's reports are being prepared for inclusion in a computerized information system to be managed by OECD.

(1) Health and Ecological Effects, and Enviromental Behavior

- a. Health Effects -- A variety of epidemiological studies, as well as studies on toxicity mechanisms, synthesis of chelating agents, and impacts on protein synthesis are being conducted.
- b. Because of the many uncertainties relating to or including subclinical effects and the effects on methylmercury toxicity, an epidemiological study is being carried out in Iraq with mothers as well as their infants who were exposed either prenatally or postnatally to methylmercury as a result of the use of mercuriated seeds for the preparation of bread. In order to adequately follow the development of these exposed infants studies will have to be continued for many (at least ten or twelve) years.
- c. Carcinogens -- Long term feeding studies with experimental animals with inorganic or aryl or alkyl mercurials have been reported. Mercurials were not carcinogenic under the conditions of the test.

(2) Current and Projected Sources, Environmental Levels, and Exposed Populations

- a. Environmental Release and Fate -- Sampling of mercurial releases at the Four Corners powerplants has identified low levels of various forms of mercury at various distances from the plant. Two additional years of activity will attempt to further refine analytical procedures, more closely follow environmental transport, and identify the ultimate fate.
- b. Mercury in a Metropolitan Area -- An EPA survey of levels and sources of mercury in environmental substances in the Washington, D.C. Metropolitan Area is in progress. A report is available in draft form.
- c. Environmental Levels -- The technical literature is being reviewed to document previous monitoring activities. The results will be evaluated for adequacy. If needs be, additional monitoring will be undertaken. The final report is available (EPA 560/6-77-03).

FDA is continuing its program for measuring mercury in the Total Diet (Total Diet studies), as well as in fish (Pesticides and Metals in Fish program).

2. Issues

A. Additional Research Needs:

(1) There is still doubt as to whether or not selenium exerts a protective effect against dietary methylmercury. So far, studies have not been conclusive. Additional studies may be required.

(2) Another possible new area for research is suggested in the following statement by NIOSH taken from an OSHA draft proposal:

"Because of the prevalence in the general population of non-specific signs and symptoms which can be associated with mercury, it is difficult, if not impossible, to establish a level at which no effects are observed. This is illustrated by studies of Smith and his co-workers, Bidstrup and her associates, Terrian et al., and Trachtenberg. Effects between 0.005 and 0.06 mg Hg/cu/m were found in these studies. The problem is further complicated because the validity of sampling and analytical methods on which the air levels are based cannot be determined conclusively; thus effects cannot be correlated with a high degree of confidence. Until better methods are established that will permit more specific identification of the effects of exposure to low levels of mercury, a specific level at which a standard should be at least as low as 0.05 mg Hg/cu/m."

(3) The environmental impact of converting from oil to coal burning needs to be determined.

3. Statutory Authority

- FDA - Food, Drug, and Cosmetic Act
Section 351 of the Public Health Service Act
- EPA - Federal Water Pollution Control Act (FWPCA), Sections 307(a) 304(b), and 203(a)
 - Federal Hazardous Substances Act
 - Clean Air Act (CAA), Section 112
 - Safe Drinking Water Act
 - FIFRA
 - Marine Protection, Research, and Sanctuaries Act
 - TSCA
- CPSC - Federal Hazardous Substances Act; Consumer Product Safety Act

4. Principal Actions/Schedules (Tentative)

A. EPA:

(1) Air Pollution Assessment - A preliminary assessment of air pollution problems associated with mercury and mercurial compounds is being prepared. When completed, a decision on the need for further study and/or regulatory action will be made.

(2) Water Pollution Assessment - Sixty-five chemicals and classes, including mercury, are being surveyed in connection with effluent discharges. Physical and chemical behavior, health and environmental effects, and sources and environmental levels will be documented over the next year. The report, including appropriate water quality criteria, is scheduled to be published by September 1978. Appropriate water quality criteria, effluent guidelines, toxic pollutant standards, and/or pretreatment requirements will then be established under the Federal Water Pollution Control Act in accordance with a court-approved schedule.

B. FDA:

(1) In 1974 the FDA established an action level of 0.5 ppm for mercury in fish and shellfish (for details see the Federal Register December 1974, 39 FR 42738). The action level was based on a tolerable daily intake of 30 ug methyl mercury (210 ug/week) and provides a tenfold margin of safety and the level of methyl mercury associated with toxic effects. The action level has been revised (1978), and the FDA will announce and action level of 1.0 ppm in fish and shellfish. This is not expected to result in the diet average intake of methylmercury from fish and shellfish to exceed 210 ug/week.

(2) Biologicals Assessment - Because 0.01% thimerosal has been demonstrated to be biologically effective as a preservative in biological products, the Bureau plans to establish a limit of 0.01% thimerosal or 50 ppm of mercury (25 ug of mercury per 0.5 ml dose) in biological products. A large volume of assay data has been collected and analyzed. On the basis of the results, narrow but realistic upper and lower limits on the assayed value will be established.

For products to which no mercurial preservative has been added, the permissible level for mercury in the product should not exceed that which is acceptable as environmental background.

It is anticipated that appropriate regulations for mercury content of biological products will be published before the end of 1978.

(3) Human Drugs - The basic authority for regulatory drugs is under Section 501 of the FD&C Act; this adulteration section of the Act prohibits the addition of a substance not needed in drug product. See also Section 502(j) on misbranding. Section 505, the new drug section, may also be used to prohibit an unneeded substance, but also may require the addition of a substance such as preservative. Depending upon the precise circumstance of either or both sections can be used to prohibit the use of a specific ingredient.

(4) Human Drugs Assessment - The Bureau of Drugs in 1970 via an internal task force reviewed the use of mercury in drug products either as an active ingredient or as an inactive ingredient such as a preservative. Broad concepts were developed to remove mercury wherever possible. While no immediate action resulted, this overview was made available to the OTC (over-the-counter) review panel for contraceptives and other vaginal drug

products. Using this data and other information located by the panel members the panel has drafted a report placing phenyl mercuric acetate in Category II, i.e., this ingredient (and other similar ingredients) are not "generally recognized as safe" (GRAS). This action was taken because of the conclusion that there was substantial evidence of potential hazard to fetuses and breast fed infants.

The panel's report is yet to be published as a proposal. The regulation (see 21 CFR 330) set forth several time-consuming steps (on the order of two years) before regulatory action could be taken.

In the meantime, because of the panel's concern being reported to industry via the official summary minutes, the major industries have voluntarily reformulated their contraceptive products to eliminate the use of mercury.

Any future actions will depend on data that would suggest that the risks were greater than the benefits.

Updates will be forthcoming as to the scope of the products that have been received, e.g., multi-dose vials have been considered where mercury compounds act as a preservative and the preservative is necessary to protect the drug from contamination.

(5) Veterinary Drugs Assessment - While mercurial diuretics and disinfectants had had historic use in veterinary medicine, they have been largely replaced by non-mercurial compounds. Unless mercurial compounds were proven through well conducted studies not to cause tissue residues, such products would be subject to regulatory action.

C. OSHA:

Revision of "Occupational Exposure to Mercury" Standard - This limit of 0.1 milligrams mercury per cubic meter of air (0.1 mg/m³) as a time weighted average (TWA) concentration based on the exposure up to a 10-hour work day and 40-hour work week.

The proposal also provides requirements for employee exposure measurement, methods of compliance, personal protective equipment, employee education, medical surveillance, recordkeeping, etc.

D. CPSC:

(1) A primary regulatory authority for the regulation of mercury is Section 2(f)(1) of the Federal Hazardous Substances Act. It may be regulated under the Consumer Product Safety Act. Products subject to the Act are elemental mercury switches, batteries, and others.

(2) Consumer Products Assessment - No CPSC regulatory action is expected in the near future. The major concern of CPSC is the presence of mercury and mercury compounds in consumer household products.

E. Current Schedule

- March 1978 - EPA scheduled to begin a hazard assessment program for mercury to determine the need for Section 8 regulation.
- Sept. 1978 - EPA scheduled to publish appropriate water quality criteria for sixty-five chemicals including mercury under the Federal Water Pollution Control Act in accordance with a court-approved schedule.
- Feb. 1979 - FWPCA Section 307(a) - Water Quality Criteria originally published by EPA in 1972; revised in 1976; and draft revision of criterion for mercury published on October 17, 1977. Current draft revision will be finalized by June 30, 1978.
- Sept. 1978 - In February 1975, EPA ordered the immediate halt to production of mercury pesticides. Subsequent to litigation, registration of mercury pesticides was allowed for several uses for which adequate substitutes have not been identified. Some of these allowed uses are for mercury compounds in: biocides for turf (golf courses and seed treatment can be produced until August 31, 1978). However, total production may not exceed the level recorded for 1973-1975. Application of these exempted mercury pesticides may continue after August 1978 until supplies are depleted.
- December 78 - FDA: Preservatives in Biologicals
Because 0.01% thimerosal has been demonstrated to be biologically effective as a preservative in biological products, a limit of 0.01% thimerosal or 50 ppm of mercury 25 ug of mercury per 0.5 ml dose in biological products is planned. A large volume of assay data has been collected and analyzed. On the basis of the results, narrow but realistic upper and lower assay limits will be established.
- For products to which no mercurial preservative has been added, the permissible level for mercury in the product should not exceed that which is acceptable as environmental background.
- It is anticipated that appropriate regulations for mercury content of biological products will be published before the end of 1979.
- December 78 - Publish final Disposition of action level for Mercury in Fish.
- Open - Publication by OSHA of revised "Occupational Exposure to Mercury" standard.

- Open - Development of a Method to Specifically Determine Methylmercury Concentrations in Fish and Other Foods.

Presently, chemical analytical procedures for measuring mercury compounds are based on the level of mercury metal present in samples of food. A recently published method for measuring specifically methylmercury in foods is undergoing collaborative study to establish test reliability so that the test may be used in future regulatory actions.

- Open - Development of an Analytical Method to Determine the Concentration of Mercury in Biologicals.

As a basis to establishing regulations limiting the levels of mercurial preservative in biologicals, FDA's Bureau of Biologics is developing a reliable method for determining levels of mercurial preservations in gamma globulin and vaccines.

5. Principal Technical Contacts

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Dr. Edward Seligmann	496-4937
Dr. Joan May	496-1853
EPA - Mr. James Kariya	755-1501
OSHA - Mr. Ching-Tsen Bien	523-7075
CPSC - Dr. Sam Molinas	492-6504
Regulations Development Work Group Coordinators	
FDA - Mr. Ronald J. Wylie	443-3480

6. Recommendations

- A. That an assessment of the health impact of an increase in future use of coal (containing mercury and mercury compounds) be conducted with the cooperation of DOE and other energy agencies.
- B. The embryotoxic and fetotoxic effects of chronic exposure of women of childbearing age to low levels of mercury compounds be determined and tolerable levels of exposure be established.
- C. The sub-clinical effects resulting from chronic low level exposure to mercury compounds be determined, and used to establish tolerable levels of exposure.

Nitrosamines

1. Background

A. Health Effects

Nitrosamines are formed by reactions between nitrous acid and amines and are characterized by the chemical grouping "N-N=O."

Many nitrosamines have been shown to be carcinogens in test animals and mutagens in selected bacterial test systems. They are very probably carcinogens in humans. However, epidemiological studies to date do not show a direct relation between exposure to nitrosamines and cancer in man.

B. Production/Use

Nitrosamines are used only in rubber processing and as intermediates in the manufacture of rocket fuel and some organic chemicals. When nitrosamines are used as intermediates, they are usually manufactured and used at the same site rather than being transported to other sites or sold to other companies. Nitrosamines may be formed in air, water, and food because the precursors (amines, nitrogen oxides, nitrates, nitrites) may be present.

FDA and USDA are monitoring the occurrence of nitrosamines in food, and EPA on the occurrence in air and water. So far as food is concerned, nitrosamines have been detected with consistency only in fried bacon.

C. Current-Status of Regulations

EPA. EPA is assessing the magnitude of the potential hazard of certain pesticides containing nitrosamines. EPA may issue an RPAR notice on nitrosamine-contaminated pesticides which exceed a specified level of risk. Pesticide manufacturers are testing their products now for the presence of such compounds.

EPA has no regulations regarding nitrosamines in air and is not planning any immediate actions. EPA does have standards for nitric oxides in air based on health effects of the oxides and not on nitrosamines. EPA will address the nitrosamine issue in its development plan for "National Ambient Air Quality Short Term Standard for Nitrogen Dioxide." EPA plans to propose the standard by February 1978.

The agency is drafting a standard for nitrosamines in ambient water supplies which is to be proposed by June 30, 1978.

EPA has sponsored two ad hoc study groups which have submitted the following reports:

"Assessment of Scientific Information on Nitrosamines,"
August, 1976, Martin Alexander, Chairperson.

"Scientific and Technical Assessment Report on Nitrosamines," November, 1976, F.G. Hueter, Chairperson.

FDA. FDA regulations provide for the use of sodium and/or potassium salts of nitrates and nitrites in smoked fish, home-cured meat and poultry, cod roe, canned pet food, adhesives used in food packaging, and boiler water. Because these salts may react with amines to form nitrosamines, FDA is concerned about their continued use.

FDA regulations also provide for certain food additive applications of morpholine. Because of the potential for the reaction of morpholine with nitrite to form nitrosomorpholine, FDA is also concerned with the safety of the continued use of morpholine.

On November 3, 1972, FDA proposed to eliminate all uses of nitrate in FDA regulated products, except home-cured products, all uses of nitrite as a color fixative, and certain uses of morpholine.

On November 16, 1973, FDA required nitrite to be packaged separately from flavorings and seasonings in curing premises, thus eliminating a problem with nitrosamine formation in such premises.

On November 11, 1975, USDA proposed to reduce or eliminate use of nitrite and nitrate in meat and poultry.

On April 22 and July 15, 1977, USDA advised FDA that nitrate and nitrite are prior sanctioned for use in red meat, but not in poultry.

On September 2, 1977, FDA determined that nitrate and nitrite in poultry are food additives and established a program for obtaining information to resolve questions regarding safe use of these additives in poultry.

On September 14, 1977, the FDA requested USDA to furnish details regarding the prior sanction USDA issued for use of nitrate and nitrite in red meat.

On October 14, 1977, USDA determined that nitrates and nitrites currently used in manufacturing cured meat products have the potential for interacting with components of the meat to form carcinogenic nitrosamines. The Agency established a program for obtaining from industry information required to resolve definitive questions about the safety of the continued use of nitrates and nitrites in such products.

FDA is planning to withdraw its November 3, 1972 proposal regarding use of nitrates and nitrites and issue a new proposal requesting information on nitrosamines in certain foods.

FDA is actively conducting investigations of nitrosamine contamination of cosmetic products. The investigations involve the analysis of a wide variety of cosmetics for N-nitrosodiethanolamine and skin penetration studies with excised human skin and in monkeys. FDA is also holding meetings with industry to discuss analytical methodology and chemistry of the formation of nitrosamines in cosmetic products. At this time FDA is not planning to conduct further carcinogenicity studies in animals.

OSHA. OSHA at this time is interested only in monitoring the efforts of the IRLG members in regulating nitrosamines particularly as related to general occupational hazards. OSHA has not committed project staff to the development of a standard for nitrosamines nor is any activity anticipated for the next several months.

FDA and USDA are working toward a uniform policy to limit the use of nitrate and nitrite (precursors of nitrosamines) in food only to those uses which are essential in inhibiting the growth of the microorganism Clostridium botulinum and its production of botulinal toxin and for obtaining the essential characteristics of cured food products.

2. Issues

- A. Is there a need for regulatory or control action relative to nitrosamines, and if so, should action be directed only at nitrosamines per se, or should standards be set for levels of the precursors: nitrates, nitrites, nitric oxides, and amines in air, water, and food?
- B. Are there tolerable levels for nitrosamines in air, water, and food, or should exposure levels be set at zero? Due to the Delaney Clause in the Federal Food, Drug and Cosmetic Act, FDA cannot set a tolerance based on risk/benefit analysis for a food additive which is a known carcinogen.
- C. Should EPA or FDA control levels of nitrosamines in water?
- D. The USDA and FDA have apparently taken the position that unless nitrosamines are preformed in food prior to ingestion, the use of nitrites in certain foods will be permitted to continue. The rationale is that only a small proportion of dietary nitrite derives from nitrite-treated foods. Is this a proper approach that could apply to air and water, or should the possibility of in vivo nitrosation be given greater consideration?
- E. Are adequate analytical methods available to determine risks?

3. Statutory Authorities

- A. FDA - Federal Food, Drug and Cosmetic Act
Section 409(c)(3), which is known as the Delaney Clause, prohibits the addition to food of any additive which is found to induce cancer when ingested by man or animal.
- B. EPA - Federal Insecticide, Fungicide and Rodenticide Act
Section 6 - Cancellation/Suspension
Section 3 - Rebuttable Presumption
- Federal Water Pollution Control Act
- Clean Air Act
Section 112 of the Clean Air Act gives EPA authority to set standards which provide an ample margin of safety in order to protect human health from hazardous air pollutants.
- C. OSHA - The Occupational Safety and Health Act of 1970 gives OSHA authority to prescribe standards such that no human will suffer material impairment of health during his/her working time for any substance while in private employment.

4. Proposed Actions/Schedules (Tentative)

The issues are as much legal as scientific. The impact of realistic exposure of nitrosamines on human health should be evaluated before specific standards are promulgated.

There are no apparent conflicts between FDA-USDA requests for data on nitrosamines in nitrite treated food and EPA's assessment of nitrosamines in pesticides and development of a short term standard for nitrogen dioxide in ambient air.

Current schedule of proposed actions:

A. EPA

- 2/78 - Proposed "National Ambient Air Quality Short Term Standard for Nitrogen Dioxide."
- 6/30/78 - Proposed standard for nitrosamines in ambient water supplies.

B. FDA

- Summer 1978 - FDA withdrawal of November 3, 1972 proposal regarding use of nitrates and nitrites and issuance of a new proposal requesting information on nitrosamines in certain foods.
- Summer 1978 - Actions on information received in response to request for data on nitrates and nitrites in poultry products. (published September 2, 1977).

5. Principal Technical Contacts

EPA - John Bachmann	8/629-5231 (FTS)
Martin Rogoff	426-2510
Leonard Guarraia	245-3042
FDA - Pete Chichilo	472-5690

6. Recommendations

- A. Policy decisions and statutory language should be clarified to clearly delineate FDA and EPA responsibility in regard to nitrosamines in water. This is necessary even while the agencies develop a consistent approach to this problem.
- B. Analytical methods for determining nitrosamines should be further developed and validated among the agencies.
- C. To maintain communication with respect to nitrosamines, all relevant information forthcoming will be exchanged with concerned agencies. Whenever any regulatory action is initiated, the Agency will attend any critical meetings or hearings conducted by the other agencies. Each Agency contact will also provide the names of technical, legal and other interested informational people within the Agency to other Agency contacts.
- D. USDA should be included in further interagency contacts relating to nitrosamines.
- E. Because the impact of realistic exposure conditions of nitrosamines on human health has not been evaluated, it is recommended that the four agencies pool their knowledge and resources regarding nitrosamines in air, water, and food and determine whether there is a need for regulatory or control action relative to nitrosamines, and if so, what form this action should take.

Ozone

1. Background

A. Health Effects

Ozone in air increases respiratory ailments and causes irritation of the eyes, nose, mouth, and throat. Possible health hazards of the reaction products formed from the reaction of ozone with organic chemicals in water are presently being assessed.

B. Production/Use

OSHA

Ozone is an unwanted contaminant released during welding operations and is also a result of electrical discharges.

EPA

Ozone is a secondarily formed pollutant. Automobile exhausts and organics released into the air combine with NO_x and sunlight to form oxidants such as ozone.

EPA-FDA

Ozone is proposed for use in treating water. It can be produced for industrial applications by the action of an ozonator discharge on air or oxygen, or produced photochemically for small-scale applications by the action of ultraviolet light on air or oxygen.

C. Current Status of Regulations

FDA

- December 1974 - Petition filed in Federal Register for American Bottled Water Association.
- June 1976 - Additional data requested.
- July 1976 - Additional data submitted.
- January 1977 - The GRAS Review Branch of the Division of Food and Color additives is reviewing a petition for affirmation of ozone for use as a chemical sterilant for bottled water. A draft of the final rule was reviewed by EPA in January 1977. Comments on FDA's rule on ozone by EPA's Dr. Joseph Cotruvo.
- September 1977 - Petitioner submitted proposed plan for determining the half-life of ozone in bottled water and the specifications of the water to be treated.
- 1978 - Action on petition awaits receipt and consideration of petitioner's survey.

OSHA

The completion of an ozone standard is being made under the Standards Completion Project.

- January 1975 - Draft Technical Standard completed; Notice of Availability
- October 1975 - Proposed Ozone Standard in Federal Register (40 FR 47309).
- January 1976 - Public comment period ends.
 - Inflationary and Economic Impact Statement for Standards Completion Projects still are not satisfactorily completed. Assessment has been in process for approximately 1 1/2 to 2 years.
 - Date for public hearing has not been set.
 - Decision was made not to proceed with any other Standards Completion Project rulemaking until the first standard becomes final.
 - NIOSH is preparing a Criteria Document with their recommended standard for ozone; scheduled to be transmitted to OSHA sometime between October 1977 and September 1978.

OPTIONS:

- a. Include ozone in a general Standards Completion Project (SCP) Standard. Many of the substance specific requirements would be deleted and replaced by nonregulatory guidelines.
- b. Promulgate ozone in a separate rulemaking in the same way as Coke Oven Emissions, Sulfur Dioxide, Lead, etc..

EPA

Revision of the ozone Criteria Document is presently underway with respect to ozone in air. The Science Advisory Board reviewed this in November 1977 and again in March 1978. Future action on ozone will be determined by the review of the document. Additionally, EPA is investigating by-products of chlorination of drinking water. A proposal was published in December 1977 stating some aspects of the problem and proposing alternatives to the use of chlorine as a disinfectant in water. One of the proposed alternatives is ozone. No use levels are offered in the proposal. EPA is investigating the possible health hazards of the by-products of the ozonization of water.

- December 1977 - Publication of proposal on limits of trihalomethane in water, alternatives to chlorine.
- February 1978 - Completion of review on ozone with respect to air.
- June 1978 - Proposed ozone air quality standard.
- September 1978 - Promulgation of ozone standard (Air).

2. Issues

- A. Advanced Notice of Proposed Rulemaking published by DOT in the Federal Register of October 6, 1977, concerns the reduction in ozone contamination in airplanes, and is in conflict with EPA. EPA has commented on this Notice. The work group concluded that contact on ozone should be established with DOT and NIOSH.
- B. Cooperation in developing standardized analytical procedures for ozone is necessary.
- C. What priority has each agency attached to its investigation and evaluation of ozone? How can conflicting priorities be reconciled?
- D. EPA's jurisdiction over ozone in both water and air vis-a-vis FDA and OSHA needs clarification.

3. Statutory Authorities

- A. EPA - Clean Air Act
 - Section 109 - National Ambient Air Quality Standards.
 - Section 111 - Standard of Performance for New Stationary Sources.
 - Section 303 - Emergency Powers.
 - Title 2 - Emission Standards for Moving Sources.
 - Safe Drinking Water Act
- B. OSHA - Occupational Safety and Health Standards
 - Section 6(b)(3) - Permanent Standards
- C. FDA - Federal Food, Drug and Cosmetic Act
 - Section 406 - Tolerances for Poisonous Ingredients in Food
 - Section 409 - Unsafe Food Additives
 - Section 410 - Bottled Drinking Water

4. Principal Actions/Schedules (Tentative)

- EPA - Early - Science Advisory Board review of ozone Criteria Document 1978 (air).
- Mid-/78 - Complete review and propose revised ambient air quality standard.
- 1/78 - Proposal to set limit of trihalomethane in drinking water; suggest alternatives to the use of chlorine for disinfecting water.
- OSHA - 9/78 - NIOSH preparing Criteria Document with their recommended standard; scheduled to be transmitted to OSHA.

No date - Ozone Standard (air) - future action pending review projected of Document; may be incorporated into a single standard.

FDA - 1978 - Publish rule on affirmation of GRAS status of ozone for use as a disinfectant in bottled water.

5. Agency Technical Contacts

EPA	- Mike Jones	8/629-5231 (FTS)
	Dr. J. Garner	8/629-2266 (FTS)
	Joseph Cotruvo	755-5643
	Ervin Bellack	755-5643
OSHA	- Scott Merkle	523-7166
FDA	- Linda Taylor	472-4750
NIOSH	- Leela Murphy	(513) 684-8207

6. Recommendations

- A. Clarify jurisdictional questions between EPA and FDA concerning the regulation of substances to be used in the treatment of drinking water.
- B. The IRLG Work Group participants agreed that cooperation and coordination of efforts are necessary. Now that contact people have been identified and areas of common interest and problems determined, each individual will maintain open communication with the other with regard to actions on ozone. No specific methods were devised for this; however, information is presently being transmitted among the three agencies. Information generated during the development of EPA's criteria document will be distributed.
- C. The IRLG Work Group should include the Department of Transportation (DOT) in future discussions and attempt to resolve different standards enforced by DOT, EPA, and OSHA on the level of ozone. DOT enforces a standard of 0.6 ppm as causing no significant health effects in airplanes, whereas EPA and OSHA enforce standards of .08 ppm and 0.1 ppm, respectively.
- D. In order to facilitate joint action, agencies should determine whether differences in priority could lead to conflicts. Presently, EPA places a high priority concern on ozone in its air program, but ozone is not a high priority matter for OSHA or FDA.

Polybrominated Biphenyls (PBBs)

1. Background

A. Production/Use:

Polybrominated biphenyls (PBBs) are industrial chemical compounds that were used primarily as flame retardants in various plastic materials produced during the period from 1970 to 1976. FireMaster FF-1, primarily composed of hexabromobiphenyl and manufactured by Michigan Chemical Company (Michigan Chemical), now Velsicol Chemical Corporation located in St. Louis, Michigan, accounts for 11.6 million pounds of the total 13.3 million pounds of PBBs produced in this country. The remaining 1.5 million pounds consist of octabromobiphenyl and decabromobiphenyl manufactured by White Chemical Corporation (White) which is located in Bayonne, New Jersey and by the Fine Organics Division of Hexcel Corporation (Hexcel) which is located in Sayreville, New Jersey (plant production site now property of Saytech, Incorporated). Although an exact figure is not available, most of octabromobiphenyl and decabromobiphenyl was exported. In 1974, the year of highest production, PBBs constituted less than one percent of the total United States market for fire retardants.

At the request of the State of Michigan, Michigan Chemical ceased production of hexabromobiphenyl in November 1974. Its inventory was exhausted in April 1975. White and Hexcel discontinued the manufacture of octabromobiphenyl and decabromobiphenyl in 1974.

In 1973, FireMaster FF-1 was mistaken for magnesium oxide and was accidentally mixed with cattle feed by Farm Bureau Services Incorporated of the Michigan Farm Bureau (Michigan Farm Bureau). The contaminated feed was then distributed to a large number of farmers in Michigan. Thousands of farm animals to which the feed was given had to be destroyed or quarantined. The extent of the health hazard to Michigan farmers who fed the feed to the livestock and to the consumers who ate the PBB-contaminated food products has not been fully evaluated.

The incident has prompted considerable investigatory research, and regulatory efforts. The Environmental Protection Agency began an environmental sampling program in the vicinity of the Hexcel and White PBB plants. Sample analysis identified PBBs in fish, plants, soil, air and water. As a result of these preliminary findings, additional investigations of the New Jersey plants were conducted by the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), and the Food and Drug Administration (FDA). EPA is conducting a monitoring study at PBB user sites to determine if significant contamination to the surrounding soils and waters has occurred. FDA found, as a result of its monitoring programs, the existence of PBBs in drugs and food that were processed in the same equipment used to grind PBBs. FDA studies further found trace amounts (0.08 parts per million maximum) of PBBs in fish in the Ohio River near the Borg-Warner Corporation, a PBB processing plant.

In November 1974, the FDA established guidelines which set the permissible tolerance level in rendered animals and poultry fat at 0.3 parts per million (ppm) and at 0.05 ppm of PBB in finished animal feeds. This action superseded the previously established levels of 1 ppm in the fat of meat and 0.3 ppm in animal feeds which the FDA established in May and June of 1974. The State of Michigan, concerned that the FDA guidelines were not sufficiently low to control the hazard from long-term accumulation of PBBs, lowered the guideline level in commercial feed to 20 parts per billion (ppb) in July 1976.

PBB contamination of the environment has caused industry, legislators, special interest groups and the public to show increased concern over the risks associated with the use of this chemical. The media have covered the PBB problem extensively in a Public Broadcasting Service documentary film, in articles in newspapers such as the Wall Street Journal and the Washington Post, and in trade journals and technical publications. In August of 1977 the House Subcommittee on Oversight and Investigations of the Committee on Interstate and Foreign Commerce held hearings on the adverse effects of PBBs. Testimony taken in these hearings indicated a need for regulating PBBs. Canada also is concerned about health and environmental problems resulting from PBB contamination and as a result has banned the manufacture and use of PBBs.

B. Environmental and Health Effect Assessment

Considerable research concerning the adverse effects of PBBs has been undertaken because of the human exposure to PBBs resulting from the accidental contamination of animal feed in Michigan in 1973 and because of the structural similarity of PBBs to the polychlorinated biphenyls (PCBs). Data show that PCBs are environmentally stable and ubiquitous, highly toxic, and bioaccumulate. More limited data on PBBs indicate that they also are environmentally stable, bioaccumulate and show a number of additional adverse effects including skin eruptions, neuropathy, teratogenicity, and alterations in liver enzyme levels. In addition, presently available information raises suspicions that PBBs may be carcinogenic.

Four assessments of the research data on the adverse effects of PBBs on health and the environment are available.

- (1) Assessment of the Hazards of Polybrominated Biphenyls by the Special Actions Group, Office of Toxic Substances, EPA, dated September 1977.
- (2) Polybrominated Biphenyls in the Environment by the Environmental Protection Service, Canada, dated September 1977.
- (3) Assessment of Carcinogenic Potential of Polybrominated Biphenyls by the Carcinogen Assessment Group, Office of Research and Development, EPA, dated February 1978.

- (4) Report of the Subcommittee on Polybrominated Biphenyls
by the Department of Health Education and Welfare Committee
to Coordinate Toxicology and Related Programs, dated April
28, 1977.

Research data and information in the following environmental effects and health effects sections are abstracted from the first three assessment documents.

(A) Environmental Effects

PBBs are persistent in the environment. Monitoring studies in 1976 revealed that PBBs were still present in 26 of the 28 cultivated fields in Michigan that had been highly contaminated two years earlier as a result of the feed incident. Additionally, soils in Michigan, where contaminated milk had been dumped, still contain PBBs at levels up to 1 ppm. The resistance of PBBs to leaching and bacterial degradation indicates that these compounds will persist for a long period of time in the soil of these fields. It also has been shown that the PBB contamination is recurring possibly from grazing farm animals which ingest vegetation contaminated with PBBs.

In a study performed by the Michigan Department of Agriculture to determine the extent of contamination of the environment from PBBs, it was learned that PBBs had accumulated in the fat of deer, rabbits, coyote, ravens, ducks, and fish in Michigan. PBBs have been detected in beef in Iowa, duck in Wisconsin, and chickens in Alabama, Mississippi, New York, and Texas.

In one study using rats, it was concluded that, in the lifetime of the animal, it would excrete only 10 percent of the total dose of PBBs ingested. The repeated exposure of living organisms to such a substance may result in bioaccumulation. It has been amply demonstrated that PBBs accumulate quickly in fish and that the bioconcentration factor exceeds 10,000. Dow Chemical Company (Dow) states in its study on the toxicology of decabromodiphenyl oxide that it has discontinued research and development on octabromobiphenyl because of the likelihood that this material will accumulate in the environment in a manner similar to PCBs. E.I. duPont de Nemours and Company Incorporated discontinued efforts to develop PBBs for use as flame retardants in synthetic fibers because of the likelihood that PBBs would accumulate in the environment in a manner similar to PCBs and because of the toxicity of PBBs.

(B) Health Effects

The high solubility of PBBs in fat results in storage in adipose tissues; the chemical stability of PBBs minimizes change to more water-soluble, more readily excretable molecules. Concentration of PBBs in adipose tissue has been confirmed by studies.

Toxicological data show that PBBs act slowly in biological systems. The acute oral LD 50 of FireMaster BP-6 (a precursor of FireMaster FF-1)

has been reported to be approximately 21.5g/kg for rats. Although this dose is very high, it is noteworthy that signs of general systemic toxicity such as emaciation occurred after the oral administration of 10g/kg.

The administration of single doses of FireMaster BP-6 (BP-6) to pregnant rats caused fetal resorption and teratogenic malformations. Liver enlargement and liver nodules were observed after the administration of a single dose of BP-6 to male rats. A single dose of BP-6 induced mixed function oxidases (MFO's) for prolonged periods in Japanese quail. The occurrence of liver nodules and the induction of MFOs suggest that PBBs may be carcinogenic.

A wide variety of adverse biological effects had been observed in many animal species after the chronic administration of PBBs. Perhaps the most significant of these effects were teratogenicity in rodents and liver nodules in rats. Particularly noteworthy from the standpoint of toxicity was the suppression of humoral immunity in guinea pigs and cell mediated immune mechanisms in mice and rats. This toxic effect is important because many chemical carcinogens are known to suppress immune mechanisms.

PBBs have been shown to adversely affect reproduction in different animals. These compounds decrease comb weight of cockerels and decrease fertility of mink, hens, and Japanese quail. PBBs increase the size of liver, thyroid, testes, heart and blood tissue in cockerels. PBBs induced fetal resorption in mice and rats and abortion in cows. Additionally, PBBs reduced the survival rate of newborn calves, mink, mice, and chicks and the hatchability of avian eggs.

PBBs have been shown to affect the circulatory system of cockerels by altering the cardiac output, heart rate, arterial pressure and total peripheral resistance.

Studies on cattle exposed to high, constant levels of PBBs reported a decrease in milk production by 50 percent, severe health problems, stillborn calves and high a mortality rate of newborn calves.

Studies of Michigan residents exposed to PBBs suggest that PBBs may be immunosuppressant and cause halogenacne and abnormal liver functions.

(C) Exposure Assessment

Air: In 1977, an estimated 1,125 lbs. per million lbs. of PBBs manufactured or used in processing were lost in air as particulate matter.

Water and Sediment: In 1977, an estimated .0046 lbs. per million lbs. of PBBs produced were discharged into sewers.

Soil: Concentrations in soils adjacent to the three PBB manufacturing plants showed:

Michigan Chemical	2,500—3,500	ppm
White	2.8—7.5	ppm
Hexcel	.040—3.1	ppm

Worker Exposure: The process by which PBBs were manufactured, dried, and packaged resulted in PBBs present in the air as vapor or dust.

Distribution In Commerce: Except for the Michigan feed accident, there is no known exposure from PBBs from their distribution in commerce.

Use: The major user of PBBs was the Borg-Warner Corp. PBBs were used as a flame retardant in acrylonitrile, butadiene, and styrene plastics. The PBBs imbedded in these plastics are considered inert. No additional PBB products are currently introduced to the market; therefore, only the PBB articles previously manufactured are in use.

Disposal: Substantially all of the total 13.3 million lbs. of PBBs produced were used in the production of flame retardant plastic products. Based on an estimated 5 to 10 years life of the plastic products, most of the PBBs produced in the United States are presently contained in useful products. Within the next five years, these PBB-containing products, such as TV cabinets and business machine housings, will be disposed of through landfills or incineration and have the potential to enter the environment. It is believed that leaching of PBBs from these plastic articles will not be a problem since a study of a similar compound, decabromodiphenyl ether (DBPE), showed no detectable amounts of DBPE in the leachate.

At sufficiently high temperatures of incineration, PBBs will break down into HBr, CO₂ and H₂O. If the plastic material is heated without combustion, however, then PBB will be volatilized without change.

2. Issues

Since PBBs are no longer manufactured, the primary issue is whether there is a need to regulate any of the PBB related activities. A secondary issue is whether the EPA should take steps to control the risk of exposure to PBBs from the resumption of the manufacture and processing of PBBs.

3. Statutory Authorities

A. To control future manufacture and processing:

- (1) Federal Register Notice informing industry and the public of EPA's intent to promulgate a Section 8(a) Reporting Rule; TSCA, Section 8(a) Reporting Rule requiring notification of intent to manufacture or process PBBs.
- (2) TSCA, Section 5, Premanufacture Notification that requires industry to notify EPA of its intent to manufacture or process PBBs in a manner or use that the EPA considers to be a "significant new use."

B. To control manufacturing and processing:

- (1) TSCA, Section 6, Regulation of Hazardous Chemical Substances and Mixtures, and Section 12, Exports, bans or restricts the manufacture, processing, import and export of PBBs.
- (2) Existing legislation controls effluents and emissions of PBBs and OSHA legislative authority to control worker exposure.
 - CWA, Section 307(a), Toxic and Pretreatment Effluent Standards, gives EPA the authority to set an effluent standard for PBBs; Section 402, National Pollutant Discharge Elimination System to control levels of PBBs in discharges.
 - CAA, Section 112, National Emission Standards for Hazardous Air Pollutants gives EPA the authority to establish PBB emission standards.
 - OSHA regulatory authority to control worker exposure to PBBs.

4. Proposed Actions/Schedule (Tentative)

- 7/21/78 - Receive Reviewed Issue Paper and Draft I of Federal Register Notice from AA/OTS
- 7/21/78 - Distribute Reviewed Issue Paper and Draft I of Federal Register Notice to other Agencies and EPA Offices
- 8/25/78 - Obtain Comments on Issue Paper and Federal Register Notice from other Agencies and EPA Offices
- 9/15/78 - Submit Final Issue Paper and Federal Register Notice to AA/OTS
- 9/29/78 - Submit Notice to Register Office
- 10/6/78 - Initiate the Writing of Section 8(a) Reporting Rule on PBBs

5. Principle Technical Contacts

EPA - Larry Dorsey	755-1188
CPSC - Joseph McLaughlin	245-1445
OSHA - Jackie Rogers	523-9225
USDA - John E. Spaulding	447-2807
NIOSH- Alexander Blair Smith	8/684-3593 (FTS)
FDA - Sidney Williams	245-1466
Frank Cordle	245-3114

6. Recommendations

A. Reporting Rule for PBBs

Since PBBs are no longer being manufactured, the hazard that formerly existed from PBBs no longer exists; therefore, there is no need at this time to control the manufacture, processing, or distribution in commerce of PBBs. If industry decided to resume the manufacture or processing of PBBs, however, health and the environment would be exposed to potentially hazardous new quantities of PBBs. For this reason, the work group is recommending that PBBs be subject to a TSCA, Section 8(a) Reporting Rule. This rule would require the notification in advance of the intent to manufacture, process, or import PBBs.

B. Substitutes for PBBs

Many of the substitutes for PBBs are structurally similar to PBBs. Since PBBs are known to adversely affect health and the environment, it is possible these substitutes may act likewise. Little toxicological information is available on these compounds; therefore, these structurally similar substitutes have been recommended to the Interagency Testing Committee for consideration for a TSCA, Section 4 Testing Rule. This rule will require that manufacturers perform and report a series of specified toxicological tests on these compounds.

Polychlorinated Biphenyls (PCB)

1. Background

A. Health Effects

PCBs have been demonstrated to induce a variety of adverse effects on the health of humans and experimental mammals. They have been found in significant concentrations in waterways and sediments throughout the world. They are a widely spread contaminant of fish and wildlife resources. Recently, they have been identified in the milk of nursing mothers throughout the United States.

B. Production/Use

Domestic production of PCB ceased in 1977. Production of PCB-filled capacitors will stop in 1978. PCB is still found in transformers for electric power conversion and on railroads, in capacitors, in a small number of mining machines, and as a contaminant in the hydraulic systems of metal forming machines.

C. Current Status of Regulations

FDA proposed lowering the existing guidelines for PCBs in certain foods in April 1977. EPA proposed marking and disposal regulation in May 1977. Both FDA and EPA are working on comments to their proposals.

2. Issues

EPA is leading an interagency work group to develop regulations mandated by Congress. Under TSCA, EPA must implement a series of rules that define the disposal and use of PCBs. The work group needs to resolve a number of issues:

- A. What level of PCB exposure should be deemed "significant?"
- B. What level of PCB exposure, if any, can be considered a reasonable risk (including some cost considerations)?
- C. Should any uses of PCBs be allowed to continue?
- D. FDA must decide what level of PCBs in certain foods should be allowed.

3. Statutory Authority

EPA - TSCA mandates the following rules:

- 7/1/77 - PCB Marking and Disposal Rules
- Open - Ban on PCB manufacturing, processing, or distribution in commerce except in a totally enclosed manner

1/1/79 - Ban on PCB manufacture

7/1/79 - Ban on PCB processing and distribution in commerce

The Administrator may authorize and/or exempt activities from the above rules if the activity does not present an unreasonable risk to health or the environment.

FDA - Federal Food, Drug and Cosmetic Act.

4. Proposed Actions/Schedule (Tentative)

2/78 - Promulgate Final EPA Regulation on Labeling and Disposal

Early 78 - Propose EPA Ban Regulations

Early/Mid 78 - Final FDA Regulation on Food Levels

Late 78 - Final EPA Ban Regulation

5. Agency Technical Contacts

CPSC - Joseph McLaughlin 245-1445

EPA - Peter Principe 755-0920

FDA - Betty Campbell 245-3092

6. Recommendations

A. Joint development of EPA/FDA regulations.

B. Sharing of all toxicological, technical, economic and other information and resources.

Radiation

1. Background

A. Health Effects

In the initial stages of the 4-agency program on radiation control, it is planned to emphasize projects related to the following four areas: (1) exposures to nonionizing radiation for which hazards are suspected; (2) the impact of increased application and new technology on occupational exposure; (3) unnecessary exposure or excessive use of radiation in the healing arts; and (4) the use of radioactive materials or other forms of radiation in consumer products.

(1) Ionizing Radiation (References, Appendix I)

Since the discovery of x-rays and radioactive elements at the end of the nineteenth century, it has been recognized that radiation produced by these sources can cause ionization to occur in exposed materials. Because of this characteristic, there was early recognition that this form of energy was capable of affecting human health. It was also recognized that exposure of humans to ionizing radiation could be used beneficially. This has led to a situation where x-rays and radioactive sources have been used for diagnostic and therapeutic purposes in medicine, while at the same time they are known to be mutagenic and carcinogenic. Thus, while ionizing radiation has many benefits, its health risks remain a health problem. Although the biologic effects of ionizing radiation are better known quantitatively than the effects of most environmental pollutants, the biophysical and biochemical mechanisms underlying these effects are poorly understood. Carcinogenesis and mutagenesis appear to be the effects of most concern, although the immune system can be seriously impaired at higher dose levels. Current standards and guides in radiation protection are based primarily on estimates of cancer and genetic risks, and thus the degree of control advocated is directly related to the scientific soundness of risk estimates. In general, it is accepted by the scientific community that if human health is protected, the biosphere also will be protected.

(2) Non-ionizing Radiation (References - Appendix II)

Light - The health effects of radiation in this portion of the electromagnetic spectrum (200 nanometers to 13,000 nanometers) may vary, depending on whether exposure is to ultraviolet (250-380) radiation, visible (380-750) radiation, or infrared (750-13,000) radiation. Our knowledge of the health effects of ultraviolet is extensive — we know that there are acute effects on the eye and skin, we know that chronic effects such as skin aging and cancer can be seen and we know the chemical and inherited photosensitization can occur in people (1,2). Recently, concern has been expressed over cataracts potentially induced by near ultraviolet radiation (3). The health effects of visible light are less well understood. At a recent symposium (4), ocular effects of visible radiation were highlighted,

with special emphasis placed upon photochemical damage mechanisms associated with retinal exposure to blue light. Complete blindness has been reported (5) from continuous exposure of piglets to phototherapy lamps. The range of effects of visible light, then, is quite broad. Infrared radiation is usually understood to present a thermal hazard (6) with all of the effects associated therewith, including frank burns. Genetic effects of infrared radiation (7) have been demonstrated, however, and a model has been proposed to account for such action (8). Still being investigated is the role of all wavelengths in the entrainment and maintenance of biological rhythms.

RF/Microwaves - Past research has established the thermal hazard, or the tissue heating effect, of microwave radiation, particularly on temperature-sensitive systems such as the vascular lens of the eye and the male gonads. An occupational exposure level of 10 mW/cm^3 was adopted by the Occupational Safety and Health Administration. There are, however, no specific exposure recommendations for the general population of the U.S.

Microwave radiation exposure standards have been established in the USSR and Eastern European countries which are one thousand times lower than the U.S. guide. However, the two limits are not strictly comparable in that the conditions for measurement differ significantly. The foreign safety levels are based on results from more extensive research programs than have existed in this country. In particular, epidemiologic and chronic, low-level exposures of animals have been conducted at power densities not known to produce thermal injury. The results suggest that the central nervous system is the most sensitive system, and effects on this system and behavior are the basis for the Soviet standard.

A number of recent reports from American laboratories suggest biologic effects on the central nervous system (behavior, neurophysiology and neurochemistry), heart and chromosomes, in addition to effects on the radio frequency (RF) heating phenomenon, from exposures to low levels ($\leq 10 \text{ mW/cm}^3$) of nonionizing radiation. The results at these low power levels suggest that the effects are apparently separate from generalized heating injury.

There is presently much public, as well as governmental and scientific, concern for the safety of microwave devices already in use and the possible environmental impact of planned microwave sources in this country. Of great concern now are effects on (a) lymphocytes (12) in animals, since these cells function in the body's immune response mechanism, and (b) permeability of the blood brain barrier. Recent data (for 13,11) also indicate that there may be power and frequency "windows" one effect of RF/microwave radiation, where this effect had previously been thought to be a function of power (14).

Ultrasound - Because of the inadequacies of past human epidemiological studies, data from laboratory studies must be examined for effects that are indicative of possible adverse effects in

humans of ultrasound exposure. Reviews of the literature (15,16,17) are available and individual experimental results are published that outline potential genetic effects (18), fetal mortality (19), birth defects (20), neuromotor deficits (21), blood stasis (22), and decreased clotting times (23). In outlining what appears to be extensive research, one must realize that very little of the data, either positive or negative, has been verified by other laboratories.

B. Production/Use

As of 1970, all of the U.S. population was exposed to low levels of radiation from atomic weapons fallout and the nuclear power industry. Approximately 130 million persons were exposed annually to diagnostic x-radiation; approximately 72 million television viewers were potentially exposed to x-radiation; another 38 million were exposed, usually at low levels with uncertain effects, to radioactive materials used for luminous dial watches and clocks, etc.; another 4 million individuals were exposed to radiopharmaceuticals; around 425,000 were exposed to therapeutic x-radiation; approximately 1/2 million persons were exposed to all other kinds of x-radiation, including occupational exposure to medical, industrial, and commercial sources and accelerator-produced radionuclides; and an indeterminate number were exposed to increased levels of exposure to natural radiation due to man's alteration of the environment.

Diagnostic x-radiation accounts for approximately 90 percent of man's exposure to manmade ionizing radiation. Apart from the sheer numbers involved, medical uses of all forms of radiation probably cost the nation well over \$6.3 billion annually, which is the estimated annual cost of diagnostic x-rays.

The presence of nonionizing radiation from manmade sources is also increasing dramatically as a result of new technology. Prior to World War II, the presence of RF/microwave radiation in the environment was negligible. Since then, electromagnetic emissions from RF/microwave frequency generators for communications, radio-navigation, military and industrial applications, diathermy, and food ovens are receiving considerable attention because of the potential public health risks. Light from manmade sources for use in industry, research, commerce, and medicine are also expanding the public health problems in the non-ionizing area. Recent extrapolation of injury data indicate that sunlamps used by the general population for cosmetic purposes cause approximately 10,000 injuries per year, primarily related to overexposure of the eyes or skin. Mercury vapor lamps used for general illumination have also been shown to emit hazardous ultraviolet radiation if the outer glass envelope of the lamps are damaged. Other ultraviolet devices include those used for entertainment, advertising, industry, and in medicine. The emissions of laser products offer many new industrial and commercial applications, but this new industry also introduces new potential for public health injury if the products are poorly designed or improperly used. Other sources of public health exposure to nonionizing radiation include the devices or equipment which emit in the ultrasonic range, such as radar transmitters and industrial and medical ultrasound products.

Knowledge of the type and amount of radiation hazards and our ability to reduce them varies markedly between the sources of ionizing and of nonionizing radiation. More is known about the biological impact of both high and low levels of ionizing radiation than about non-ionizing radiations.

The general strategy to reduce or eliminate radiation exposure and its resultant hazards has several facets. First, a data base sufficient to characterize a problem is developed: Bioeffects studies elucidate the mechanisms of physical interaction and biological results; surveys and studies of usage and distribution of radiation define the actual or potential exposure of persons to radiation; epidemiological studies evaluate direct public health effects, and instrumentation studies help to define a feasible means of quantitating the radiation, the dose, and a feasible design for control.

Once the assessment of exposure, risk and health effects is quantitated, priorities are assigned considering both the magnitude of hazard in health terms (both in quality of life and dollar cost) and the potential solutions that are available and their relative cost (in both health care and dollar resources).

Effective governmental programs to resolve problems involve exposure and facility standards, licenses or permits, Federal guidance to Federal and State agencies; equipment regulations; guidelines or recommendations that will impact on behavior; and educational programs that affect the manufacturer and distributor of equipment or products, the user, providers of health care and the consumer. In addition, the Federal government provides assistance to State radiological health agencies, an effective and relatively economical means of action to implement radiation programs.

2. Issues

A. The scope of a national radiation protection program is so broad and involves so many agencies that it has been agreed to limit the scope of this plan initially to those areas which are more likely to involve two or more of the 4 agencies of the IRLG. Therefore, the plan emphasizes the following four areas:

- (1) Nonionizing radiation
- (2) Occupational exposure
- (3) Radiation in the healing arts
- (4) Radioactive material in consumer products

The hazards associated with exposure to high levels of ionizing or nonionizing radiation are well established; however, the effects of low levels of exposure are not well defined and generally are difficult to determine. The principle of "As Low As Reasonably Achievable" (ALARA) is applied in most nonionizing radiation protection programs based upon the conservative assumption that effects on the population may be directly proportional to the dose. There is a need for additional information on the biological effects

of low levels of radiation especially with respect to light, microwaves, and RF radiation and ultrasound.

B. Ionizing Radiation Assessment (References - Appendix I)

(1) According to a recent compilation and analysis of health risks associated with radiation, an additional exposure of the U.S. population of 5 rem per 30 years could cause roughly 3,000 to 15,000 cancers annually. The most likely estimate is approximately 6,000 cancer deaths annually, an increase of about 2 percent in the spontaneous cancer death rate which is an increase of about 0.3 percent in the overall death rate. (1)

The most tangible measure of total genetic damage is probably "ill-health." It is thought that between 5 percent and 50 percent of ill-health is proportional to the mutation rate. Using a value of 20 percent and a doubling dose of 20 rem, it can be calculated that a 5 rem radiation dose per generation would eventually lead to an increase of 5 percent in the ill-health of the population.

If in fact, any level of radiation will cause some harm and if in fact, entire populations are being exposed to additional manmade radiation, then it becomes necessary to quantify risks, that is, to estimate the frequency of effects in order to make rational decisions about radiation protection and the most efficacious use of ionizing radiation.

(2) Environmental Effects - In regard to possible effects of ionizing radiation on the environment, if the guidelines and standards are accepted as adequate for man, then it is highly unlikely that populations of other living organisms would be perceptibly harmed. Nevertheless, ecological studies might be improved and strengthened and programs put in force to answer the following questions about release of radioactivity to the environment:

- a. how much, where, and what type of radioactivity is released;
- b. how are these materials moved through the environment;
- c. where are they concentrated in natural systems;
- d. how long might it take for them to move through these systems to a position of contact with man;
- e. what is their effect on the environment itself;
- f. how can this information be used as an early warning system to prevent potential problems from developing?

C. Nonionizing Assessment (References - Appendix II)

(1) Health Effects

a. Light - The only available risk assessments in this area relate to solar ultraviolet radiation. Pursuant to assessment of the impact of future aircraft, the biological implications of increased solar UV radiation have been presented (24). Pursuant to assessment of the impact of fluorocarbons released into the atmosphere, the biological effects of ozone reduction have been reviewed (25,26). In all cases, quantitative data appear to be limited to incidence of non-melanoma cancers. Still left to be considered is the occurrence of malignant melanomas. One final factor that has yet to be evaluated is the importance of photosensitive populations in estimated risk.

Sufficient data are not available to establish quantitative risk assessments to be considered for other sources, their emissions, and the populations exposed. The ultraviolet radiation from sunlamps, broken mercury vapor discharge lamps, germicidal lamps, phototherapy lamps, and even fluorescent lamps can result in the acute and chronic effects noted earlier. The degree of effect will depend upon exposure, distance, and duration, and the effectiveness of safety measures already instituted. Concerns over the potential hazards of radiation in the blue portion of the visible spectrum involve almost every source of light known. With almost the entire population exposed, even a small hazard, if present, would be significant when it involves such large numbers of people. The hazards of high intensity sources of visible light such as searchlights, flash units, strobe lights, and lasers involve potential exposure of only a part of the population, but the acute dangers of eye damage are of enough concern to have resulted in several safety standards. Other risk assessments that remain to be done are in the area of medical exposure. Infrared radiant warmers, ultraviolet and visible radiation phototherapy devices, ultraviolet radiation dental devices, and even visible radiation-emitting operating room lamps are all yet to be completely evaluated for safety and effectiveness.

b. RF/Microwave - During a discussion at an international meeting (9) on biological effects of microwaves (1 meter to 1 millimeter in wave length), it was suggested that microwave intensities be divided into the following three ranges:

- "(i) High intensities at which distinct thermal effects occur; in many instances such effects may be hazardous. These intensities range from 10 mW/cm^2 upwards (region of thermal effects).
- "(ii) The range of subtle effects from about $1\text{--}20 \text{ mW/cm}^2$
In this range in part weak thermal but noticeable effects exist; direct field effects, as for example the phenomena of hearing pulsed fields; and perhaps, a group of other effects of a microscopic nature, details of which are at present unclarified (region of subtle effects or intermediate region).

"(iii) The region at intensities below 1 mW/cm^2 . In this region thermal effects are improbable (region of nonthermal effects)."

While this does not represent a risk assessment per se, it does represent the extent to which researchers appear to be willing to categorize RF/Microwave effects.

c. Ultrasound - Attempts have been made to use the available bioeffects data to construct curves or limits which delineate safe levels, threshold levels, or lowest levels for reported biological effects (15,16,17). The value of such graphic presentations of isolated data is questionable, because although very few of the data points represent threshold studies, these curves and graphs have been widely interpreted as representing a "safe" level of ultrasound. Such an interpretation disregards the fact that a threshold level must be based on studies designed to measure threshold effects and the fact that "thresholds" tends to decrease as more sensitive endpoints are studied and more sensitive means for measuring these endpoints are utilized. In fact, there are several recent studies reporting effects below the levels of any of the aforementioned curves (21,27, 28,29). The overall belief in this country is, however, that ultrasound is safe as presently used in medical practice. Given the evidence, this belief may not be warranted.

(2) Environmental Effects

a. Light - The largest environmental source of light is the sun, so it is not surprising that solar radiation in this part of the spectrum has the major effect on the environment. Many effects are beneficial. In fact, the recent International Congress on Photobiology took as its motto: *lux vita est*. On the other hand, this source of environmental radiation can be hazardous.

b. RF/Microwave - A recent EPA report (3) stated: "Although environmental levels of nonionizing radiation were negligible before the 1930's, virtually every American is now exposed. Sources have proliferated in number as well as power; in the ranges of primary interest, the radiofrequency (10 MHz to 200 MHz) and microwave (300 MHz to 300 GHz) frequencies, the environmentally significant sources include:

- radio and television broadcast stations
- radars
- satellite communications system earth terminals
- point to point microwave communications
- mobile communications systems
- microwave ovens
- industrial heating equipment."

c. Ultrasound - Airborne ultrasound is produced by many commercial and home protective devices. The effects of such radiation have not been studied sufficiently to allow discussion.

3. Statutory Authority

Several Federal, State, and Municipal agencies have legislative authority for radiation protection. Therefore, close liaison between these agencies must be maintained, and efforts continued to coordinate the approach to a national radiation protection program.

- CPSC - Consumer Product Safety Act (Radium)
 - Federal Hazardous Substances Act
- EPA - Atomic Energy Act
 - Clean Air Act
 - Federal Water Pollution Control Act
 - Resources Recovery and Conservation Act
 - Safe Drinking Water Act
 - Marine Resources and Conservation Act
 - Toxic Substances Control Act
 - Solid Waste Disposal Act
- FDA - Food, Drug and Cosmetic Act
 - Public Health Service Act
- OSHA - Public Contract Act
 - Occupational Safety and Health Act
 - Contract Work Hours and Safety Act
 - Longshoreman and Harbor Compensation Act

4. Principal Actions/Schedules (Tentative)

A. Actions to Date

The national program for radiation protection has been achieved through complementary regulations and guidelines of Federal, State, and local agencies, and guidelines of voluntary standard-setting organizations such as the International Council on Radiation Protection and Measurements (ICRP), International Atomic Energy Agency (IAEC), and the National Council on Radiation Protection and Measurements (NCRP). The regulations and recommendations have generally applied to one or more of the areas listed and described below:

- Personnel exposure guides
- Radioactivity in the environment
- Use of radioactive material
- Electronic product radiation

(1) Federal Agency Guides and Radioactivity in the Environment

Broad radiation exposure guides for Federal agencies are the responsibility of EPA under the Federal Radiation Council responsibilities transferred to EPA under the Executive Reorganization Plan No. 3 in 1970:

"... the Federal Radiation Council, a Presidentially appointed, Cabinet level group formed 'to advise the President with respect to radiation matters, directly or indirectly affecting health, including guidance to

Federal agencies in the formulation of radiation standards' (73 Stat 690)."

The FRC published eight reports, the latest in 1967, which provide exposure guidelines to Federal agencies for application to radiation workers and the general population in the area of ionizing radiation. Since the transfer of the FRC responsibility to EPA, the EPA Office of Radiation Programs has proposed Guidance on Dose Limits for Persons Exposed to Transuranium Elements in the General Environment (42 FR 60956), developed in cooperation with several other agencies. Guidelines for emergency response planning, and regulations for radioactivity in drinking water were also issued. In January 1977 (42 FR 2858) EPA published new final standards for planned releases from the uranium fuel cycle. These apply to uranium mills, chemical conversion plants, enrichment facilities, fuel fabrication and processing plants, and nuclear reactors. EPA also coordinated with certain other Federal agencies the drafting of radiation protection guidance for diagnostic x-rays in Federal health care facilities which have recently been approved by the President.

(2) Production and Use of Radioactive Material and Consumer Products

The Nuclear Regulatory Commission has responsibility for the licensing and regulation of byproduct source, and special nuclear material. Thus, NRC must implement radiation protection standards, both by defining specific requirements in the licenses for plants, and individuals, and by enforcing them. The NRC also may delegate authority to the states for the licensing and regulation of by-product, source, and special nuclear material in amounts less than required to form a critical mass. At the present time, twenty-seven states have accepted this transfer responsibility. The regulations issued by NRC are contained in the Code of Federal Regulations, Title 10, Chapter 1.

The Food and Drug Administration has authority to regulate the manufacture, distribution, and use of radiopharmaceuticals and medical devices containing byproduct or naturally-occurring radioactive material, and controlling radioactive material which may occur in foods, drugs, cosmetics, or devices. Regulations pertaining to these matters are contained in the Code of Federal Regulations, Title 21, Chapter 1. Because of overlapping jurisdiction with the Nuclear Regulatory Commission, the two agencies have collaborated closely in the development and promulgation of related regulations. The two agencies are currently negotiating an interagency agreement for the control of radioactive material involving medical devices. The FDA also have authority to issue recommendations to State agencies and others on the safe use of radioactive material and on emergency action for health care personnel, and to protect against unsafe foods and animal feeds.

The Consumer Product Safety Commission has authority to regulate consumer products containing naturally-occurring or accelerator-produced radioactive materials, but has not chosen to exercise this authority to date.

The Occupational Safety and Health Administration has established regulations to protect the worker from the hazards of ionizing radiation. These regulations are contained in the Code of Federal Regulations, Title 29, Part 1910.96, et seq., 1926.54, and Title 41, Part 50.204. To some extent, they overlap the regulations of NRC but are not inconsistent with the NRC regulations. OSHA also has authority to permit transfer of regulatory responsibility to State agencies, provided the State regulations are equivalent to those of OSHA.

Guidelines recently have been developed by Federal and State agencies for the regulation by states of naturally-occurring and accelerator-produced material. Also, the Bureau of Radiological Health, FDA, coordinates the periodic revisions to the model state regulations for control of radiation. This model includes revisions to the NRC regulations for the control of byproduct, source, and special nuclear material. Surplus products containing radioactive material are regulated by the General Services Administration under Code of Federal Regulations, Title 41, Chapter 101. The GSA collaborates with the NRC and FDA in the development of these controls.

(3) Electronic Product Radiation

The FDA conducts an electronic product radiation control program which includes the development and enforcement of performance standards for the manufacture of products, and recommendations for the quality assurance and use of the products. Radiation protection standards have been established for television sets, cold cathode gas discharge demonstration tubes, cabinet x-ray and baggage x-ray products, microwave ovens, diagnostic x-ray equipment, laser products, and ultrasound therapy equipment. Recommendations have been issued for use of gonadal shields in x-ray procedures, recommendations against continued mass x-ray screening for cardiopulmonary diseases, and procedures for use of laser products in educational facilities.

The FDA also coordinates the biannual revision of model state regulations for radiation control by Federal and State agencies. The FDA also has authority to take action against the manufacturer of an electronic product which has a defect relating to radiation safety, irrespective of whether a regulatory standard has been issued for that product, provided the product was manufactured after October 18, 1968. As indicated under the discussion of radioactive materials control (2), the FDA collaborates with GSA in development of appropriate regulations to control the distribution of surplus electronic products of Federal agencies under 21 CFR 101.

State and Territorial agencies have authority to protect the public health and safety from electronic product radiation. However, most

states protection programs are limited to enforcement of regulations for products which emit ionizing radiation. Forty-three states have comprehensive regulations for ionizing radiation products, but less than 5 have regulations for nonionizing sources, such as lasers, microwave ovens, and industrial and medical microwave, UV and ultrasound equipment.

B. Schedules (Tentative)

Radiation protection activities of the 4 agencies in the areas defined by the scope of this plan (Section IIA) which are planned for the current fiscal year are briefly summarized below:

(1) Nonionizing Radiation Sources

a. EPA - Federal Exposure Guidance

EPA is considering the need for Federal guidance for environmental exposure to nonionizing radiation. It is conducting environmental assessment and biological effects research programs to gather the information necessary to make this decision.

b. Notice of Intent to be published 9/1/78 FDA - Recommendation for Phototherapy Device

FDA is developing recommendations to apply to the performance of phototherapy equipment used in conjunction with the drug psoralen to treat patients afflicted with psoriasis. The radiation sources that presently exist consist of banks of lights arranged to give a uniform exposure to the patient. The exposure is largely limited to that portion of the ultraviolet spectrum between 320 and 380 nm. As with those portions of the erythral region found in the solar spectrum, overexposure can cause skin cancer. Even for that portion of the ultraviolet spectrum used in the treatment, there are research data indicating that cellular death and cellular mutation can occur after exposure.

c. Notice of Intent published 6/19/75, Proposed Rule published 12/30/77, Final 7/78 FDA - Regulatory Standard for Sunlamps

Sunlamps usually emit a considerable amount of visible light. However, they are also designed to emit invisible light, particularly at wavelengths shorter than 320 nanometers. Published literature on the effect of this wavelength region has indicated a strong link between chronic exposures to this ultraviolet radiation and the induction of skin cancers. Available data compiled by the National Electronic Injury Surveillance System (NEISS) of the Consumer Product Safety Commission also show sunlamp-related injuries occurring nationwide. The standard under development by FDA since 1975 is intended to allow continued use of a sunlamp product and yet to minimize the danger of injury. This purpose is achieved through the pro-

visions of safety performance criteria in the standard including the limitation of shorter wavelength emissions, more adequate warnings, requirement of special lamp base and a timer to control the duration of the exposure.

- d. Proposed Rule published 4/21/78, Final 8/78 FDA - Regulatory Standard for Mercury Vapor Lamps

FDA is promulgating a regulatory standard for mercury vapor and metal halide lamps used for general illumination in school gymnasiums, stores, industrial facilities, streets, and highways. A potential radiation hazard associated with the use of such lamps occurs when the outer bulb of the lamp is broken while the inner arc tube of the lamp continues to operate. This results in the emission of hazardous short wavelength ultraviolet radiation. The standard is intended to reduce the possibility of injuries by requiring that some performance safety feature be incorporated into the lamp so that it will cease operation within a short period of time following the breakage of the outer envelope. Lamps without such a safety feature will be limited to restricted uses only. Further, adequate information for the safe use of both types of lamps is also required to be provided to the user.

- e. Notice of Intent published 6/3/75, Proposed Regulation by 6/78, Final 11/78 FDA - Regulatory Standard for Microwave Diathermy

FDA will promulgate this standard to provide general requirements for microwave diathermy products to assure that to the extent that safety and performance can be controlled, microwave diathermy products are effective for their intended use and the risk of injury to patient and attending personnel is minimized. The proposed standard includes provisions on minimum microwave radiation output to achieve therapeutic heating, limits on microwave leakage, product interlocks and controls, product performance, labeling, warnings and user instructions and test requirements.

- f. Notice of Intent 6/15/78 FDA - Regulatory Standard or Recommendations for Diagnostic Ultrasound Equipment

FDA is considering the need for regulations or recommendations for ultrasound equipment. Diagnostic ultrasound equipment is used widely with little evidence of the degree to which human exposure levels may be harmful, especially to the developing fetus. A Notice of Intent has been developed covering diagnostic ultrasound equipment. The notice will announce the possible development of standards and/or recommendations related to the manufacture and use of these devices. There is insufficient basis at present to take regulatory action in this area and so the Notice of Intent will include interim guidance. The guidance will encourage manufacturers to employ the lowest power levels practicable and will caution against unnecessary exposure to patients and others. A decision will be made on future strategy after

analysis of comments from the Notice of Intent, and further evaluation of the potential problem.

- g. Proposed Rulemaking 6/14/76, Final Rule 2/17/78
FDA - Regulatory Standard for Ultrasound Therapy Equipment

Ultrasound therapy equipment used primarily for deep tissue heating often is incapable of delivering a prescribed dose with adequate precision. Also, necessary user and service information is either absent or incomplete. The standard being promulgated by FDA addresses these problems.

- h. Notice of Intent 5/1/77, Proposed Rule early 78,
Final mid-78 FDA - Amendments to the Performance
Standard for Laser Products

The experience of FDA in the administration of the FDA laser standard since it became effective on August 2, 1976, indicates that some provisions of the standard may need to be clarified. These changes would reduce, in most cases, the burden on affected manufacturers without compromising the public health. Technical changes would be made in the measurement provisions, more flexibility would be permitted in labeling, and allowance would be made for the unlikelihood of a potentially dangerous eye exposure to low-level stationary and rapidly scanning laser radiation.

(2) Occupational Radiation

- a. Proposed in Federal Register 9/78 EPA and OSHA - Exposure Guidance

Revised Federal Guidance for Occupational Exposure is in the final stages of preparation.

- b. 6/78 FDA, NRC, EPA, States - Suggested State Regulations

State radiation control programs are essential to effective national radiation protection because they complement Federal controls to provide protection in areas where Federal agencies have no jurisdiction. The Suggested State Regulations for Control of Radiation was first prepared in 1962 and is periodically updated. As a model code, it assists the States in developing their regulations and encourages uniform regulations among states to complement Federal regulations (e.g., in areas beyond certain Federal regulatory authority as in the user area). This is a cooperative project of the Conference of Radiation Control Program Directors (representing the State and local agencies), FDA, and other Federal agencies with responsibilities in radiation control (including the Nuclear Regulatory Commission and the Environmental Protection Agency). The Model State Regulations is not published in the Federal Register, but a Notice of Availability is prepared so that the information may be made available to interested persons.

(3) Ionizing Radiation in the Healing Arts

- a. EPA and FDA - Implementation of New Federal Guidance for Use of X-Rays in the Healing Arts

Several programs will be initiated by Federal agencies to implement the new guidelines to Federal agencies signed by the President on January 26, 1978.

- b. Notice of Intent to be published 3/1/78 FDA - Recommendations Concerning Mammography Screening

Mammography is a widely used procedure for the detection of breast disease, particularly cancer. However, because of the associated radiation exposure, FDA scientists raised a concern over whether the possibility of radiation-induced cancer of the breast may outweigh the benefits of mammography. Mammography screening of the general population of asymptomatic women has been recommended by various organizations including the American Cancer Society and the American College of Radiology. Because of the potential cancer risks, noted above, NIH recently convened an expert committee to review these issues and to develop guidelines for the mammography screening projects being supported by NCI. A Federal Register "Notice of Intent" (NOI) will be published by FDA which will seek to obtain information and opinion concerning such questions as the population to be screened, the usefulness of a base-line mammogram, etc. Interim guidelines will also be proposed as part of the NOI. These will be based primarily on the recommendations made by the NIH expert committee.

- c. Notice of Intent to be published 9/10/78
FDA - Quality Assurance Recommendations in Dental Radiography

The purpose of this project is to consider measures to correct the problem of overexposure and underdevelopment in intraoral dental radiography. Several ongoing programs by FDA in the dental area have indicated that radiation exposures in dental radiography are frequently higher than that necessary to obtain good diagnostic films. This project will result in recommendations by FDA (and educational programs implement those recommendations) which will help alleviate the problem.

- d. Notice of Proposed Recommendation 7/15/78, Final 3/1/79
FDA - Recommendations for Post-Treatment Dental Radiographs

A practice which appears to be on the increase is the requirement for post-treatment dental radiographs by third party carriers as evidence of treatment. The only function of radiographs taken for this purpose is to provide third party carriers with a means of monitoring treatment claims to reimbursement. Proper justification for the application of radiation to humans requires that there be some potential

benefit to the individual receiving the examination. Post-treatment radiographs, however, are not always needed for patient management. It is likely that this project will culminate in recommendations stating that post-treatment radiographs should not be taken merely as evidence of treatment.

- e. Notice of Intent to be published 8/78
FDA - Recommendation for Routine Chest X-Ray Screening for Cardiopulmonary Disease

FDA is evaluating the use of chest x-ray examination as part of routine screening programs in the detection of cardiopulmonary disease. Numerous studies have shown that routine chest x-ray screening of asymptomatic persons for certain types of pathology is neither efficacious nor cost-effective.

A Notice of Intent (NOI) will be published by FDA in the Federal Register about August 1978. After analysis of the response to the NOI, a program decision will be made as to the course of action to pursue.

- f. Notice of Intent to be published 9/78 FDA - Recommendations for Diagnostic Examinations

There exists a considerable range in the entrance skin exposure and the resulting organ doses for the same x-ray procedure conducted at different medical facilities and often within the same facility. Radiation exposure recommendations are being investigated by FDA that will permit radiologists, radiation protection personnel and others to evaluate exposure values used in a given facility. Following the analysis of the comments generated by the Notice of Intent (NOI), a program decision will be made as to the course of action to pursue.

- g. Notice of Intent 9/2/78 FDA - Recommendation for Utilization of Skull Radiography Following Trauma

Numerous discussions in the literature and several clinical studies support the contention that the number of x-ray examinations of the skull for trauma could be reduced by as much as 40 percent without adversely affecting the quality of health care. Preliminary recommendations are expected to be published in a Notice of Intent about September 2, 1978. Following the analysis of the comments generated by the Notice of Intent, the program will be reviewed and a decision made concerning its future.

- h. Notice of Intent 5/78, Proposed Recommendation 8/1/79,
Final 4/1/80 FDA - Recommendation Advocating Use of Improved X-Ray Intensifying Screens

Recent advances in the manufacture of x-ray intensifying screens offer the opportunity for significant reductions in x-ray

exposure to patients for many radiological examinations. The new generation of phosphor materials could enable the performance of many radiological examinations with exposure reductions of one-half or more over previous imaging systems without loss of image quality. The purchasers and users of intensifying screens should become aware of the potential benefits of these new systems and should use them where appropriate. It is proposed to develop a Food and Drug Administration radiation protection recommendation designed to encourage the rapid adoption of these imaging systems.

Such a recommendation, supplemented by performance data on the new intensifying screens, could provide the incentive for facilities to use these newer imaging systems sooner than otherwise would occur.

- i. Notice of Intent 3/22/77, Proposed Recommendation 5/79
FDA - Recommendations or Regulations for Radiation Therapy Equipment

Approximately half of all new cancer patients receive ionizing radiation therapy during the course of their treatment. While the physical characteristics of therapy devices vary widely, there is a general need for accurate dose delivery. Problems related to accurate dose delivery are related to both equipment and personnel inadequacies. Such problems might be alleviated by the development of standards and recommendations.

The Notice of Intent published by FDA announced the possibility of future actions in the form of regulatory standards and/or recommendations related to ionizing radiation therapy equipment used primarily in the treatment of cancer. There was considerable interest and helpful suggestions reflected in the response to the Notice of Intent. After analyzing the comments, decisions will be made by FDA about future strategy.

- j. Notice of Intent 2/14/78 FDA - Recommendations Concerning
Radiation Therapy for Benign Diseases

Ionizing radiation continues to be used for treating a variety of benign diseases which, in some cases, may better be treated by other modalities without the risk of radiation exposure. The development of recommendations by FDA on this subject may have a great impact on the use of ionizing radiation where it is not warranted.

A Notice of Intent announces the agency's intent to develop recommendations related to the use of ionizing radiation for the treatment of benign (noncancerous) conditions. A final decision on the need for a recommendation will be made in September 1978.

- k. Notice of Intent 1/9/78, Proposed Guidelines 9/25/78,
Final Guidelines 2/26/79
FDA - Emergency Radiation Dose Limits Related to Health and

Safety of Ambulance Services, Hospital and Other Health Care Personnel

Interagency responsibilities for Radiological Incident Emergency Response Planning, Fixed Facilities and Transportation Accidents published in the Federal Register (FR 59191) stated that HEW is responsible for "issuance of guidance on emergency radiation doses related to health and safety of ambulance services, hospital and other health care personnel, in cooperation with EPA." The guidance will establish dose limits for emergency medical personnel for planned and unplanned lifesaving actions during the transportation and treatment of persons contaminated with radioactivity. Recommendations will be based on a review of national and international standards relevant to this matter. They will be consistent with present radiation risk and effects information and based on the principle of avoiding unnecessary radiation exposure when possible and that any radiation exposure should be balanced by commensurate benefit.

1. Notice of Intent 8/78, Proposed Guidance 10/1/79, Final Guidance 5/30/80
FDA - Nuclear Medicine Quality Assurance of Scintillation Cameras

Quality assurance procedures, which include quality control procedures, are needed broadly in nuclear medicine to assure maximum benefit from nuclear medical techniques, consistent with obtaining high quality images at minimum cost and minimum radiation dose to the patient. The need for quality assurance procedures has been recognized by several professional organizations and the FDA. Activities in this area have included sponsorship of a workshop series on quality assurance for scintillation cameras, and publication of a "Workshop Manual" and a report, "Quality Control for Scintillation Cameras."

Voluntary recommendations, to be based on FDA technical reports, will be developed in cooperation with representatives of professional, public and private groups that have an interest and knowledge in the field. These recommendations, therefore, would represent a consensus of expert opinion upon which individual practitioners and allied health personnel can rely and would be implemented through educational programs and cooperative activities with professional organizations and State health agencies.

- m. Notice of Intent 10/18/77. Decision on publication of voluntary recommendations will be made in late 1978.
FDA - Nuclear Medicine Evaluation of Diseases of Thyroid Gland Recommendations

Over the past twenty years, increased attention has been drawn to the association between ionizing radiation and the development of nodules and cancer of the thyroid gland. It is prudent

therefore to minimize radiation exposure to the thyroid when clinical information will not be compromised. The FDA is seeking guidance on the need to formulate voluntary recommendations to encourage techniques in nuclear medicine which would lower or eliminate patient radiation dose in thyroid studies. Comments on the Notice of Intent (NOI) (42 FR 55649) and results of comparative efficacy studies of radiopharmaceuticals used in the nuclear medicine evaluation of the thyroid will be considered in evaluating the need for publication of voluntary recommendations in this area.

- n. Notice of Intent 9/30/78, Proposed Recommendation 6/30/79,
Final Recommendations 12/30/79
FDA - National Standards for Medical Radiation Technologists

Inadequate radiation protection practices on the part of allied health radiation users contribute to unnecessary patient exposure. According to available x-ray technologist performance data, the lack of effective radiation protection practices is particularly evident in noncredentialed individuals. Even among the credentialed groups, little uniformity exists in the standards enforced through public regulation or in private credentialing processes. Varying requirements lead to varying levels of job proficiency and, ultimately, variability in the quality of radiological health care provided. The need for national qualification standards is based on the fact that between 1/3 and 1/2 of the estimated 130,000-150,000 operators of medical radiation equipment are exposing patient consumers to medical radiation without ever having demonstrated a level of competence in the use of radiation. The goal of FDA is to bring all medical radiation technologists into a credentialing system, thereby reducing unnecessary medical radiation.

A Notice of Intent (NOI) will be published to announce that FDA will be establishing recommended qualifications for medical radiation technologists. The NOI will solicit professional and public input about existing practices of credentialing, the need for uniform national standards, and possible approaches for ensuring that all medical radiation technologists demonstrate a certain level of competence in conducting medical radiation examinations.

Information obtained from the NOI and through consultations with the professions and others, will serve as the basis for formulating Recommendations and Qualifications for Medical Radiation Technologists. Initial recommendations will be directed to diagnostic radiation technologist qualifications. Subsequent recommendations will address qualifications for radiation therapy and nuclear medicine technologists.

- o. FDA - Amendments to the FDA Diagnostic X-Ray Standard

The diagnostic x-ray standard is a comprehensive regulatory performance standard covering the manufacture and assembly

of ten major components of a diagnostic x-ray system. It affects the factory-based manufacturer of each component and the way in which the component is assembled into old or new x-ray systems. Thus it applies to large manufacturers and to small assemblers. Through several programs, the FDA is continually evaluating the standard, and its impact on public exposure to radiation, technical innovations and cost of medical care. The results of these studies and the compliance program point out the need for amendments. For purposes of simplicity, and because of specialized interest, these amendments are usually limited in scope and initiated as the need arises. The following are under development:

- o Notice of Intent published in the Federal Register 3/30/76
Notice of Proposed Rulemaking 1/1/78
Final Rule 5/1/78
Amendments to Section 1020.30, including recodification of Section 1000.16

These amendments will codify various interpretations and advisory opinions under which the Bureau of Radiological Health currently operates.

- o Notice of Intent 4/1/77
Notice of Proposed Rulemaking 2/1/78
Final Rule 7/1/78
Amendments Concerning X-Ray Beam Limitation

These amendments would revise and simplify the requirements for positive beam limitation (PBL) contained in Section 1020.31 (e)(2). In addition, provisions for overriding automatic x-ray field adjustment systems on fluoroscopic x-ray equipment will be addressed and a warning label required. The changes in the PBL requirements would allow more flexibility in the conditions under which PBL is required, and should promote upgrading of old equipment.

- o Notice of Intent 9/30/76
Notice of Proposed Rulemaking 9/1/78, Final Rule 2/1/79
Amendments Concerning Tomographic Systems

Computerized tomographic (CT) x-ray systems are diagnostic x-ray systems which represent a major new technical breakthrough, not available when the standard was issued. Although some provisions of the standard are appropriate for CT systems, it is recognized that other requirements may not be appropriate for such complex equipment, and that additional requirements may be necessary to assure adequate public health protection. This is at an early stage of development.

- o Notice of Proposed Rulemaking 1/1/78, Final Rule 5/1/78
Amendments to the Diagnostic X-Ray Equipment Standard

Certain of these amendments will codify various interpretations and advisory opinions under which the FDA currently operates or will clarify the intent concerning provisions of the standard.

- o Notice of Proposed Rulemaking 7/78, Final Rule 1/79
Beam Quality Amendment for Dental X-Ray Systems

The beam quality amendment for dental x-ray systems is needed to reduce patient exposure resulting from the use of low kilovoltage dental x-ray systems.

- p. Notice of Intent 12/15/75, Notice of Proposed Recommendation 8/1/78, Final Recommendation 3/1/79
FDA - Recommendation for X-Ray Exposure of Women of Childbearing Age

For years physicians used elective scheduling systems to avoid possible irradiation of a fetus or embryo in utero. However, there are several limitations to such systems. For example, they do not address the question of women known to be pregnant who are also candidates for abdominal radiographic examinations. Also, if improperly applied, elective scheduling systems may simply postpone the irradiation of a fetus to the very radiosensitive period of organogenesis while delaying important diagnostic tests for the mother. The guideline to be proposed by FDA will address and explain three particular points in an effort to reduce this risk. It will advise physicians: (a) to ascertain whether their female patients are or could be pregnant, prior to ordering abdominal radiological examinations; (b) to utilize modified or limited studies when possible for female patients who are likely to be or who are definitely pregnant, as a means of reducing fetal exposure; and (c) to use alternative procedures for radiological examinations when appropriate.

- q. Notice of Intent 5/7/76, Proposed Recommendations 5/78
Final Recommendation 1/79
FDA - Recommendation for Quality Assurance Programs in Diagnostic Radiology Facilities

Studies indicate that problems exist in diagnostic radiology facilities which can lead to unnecessary exposure and poor quality images. The studies also suggest that many of these problems can be alleviated by quality assurance programs. Studies have also proven (e.g., University of Alabama at Birmingham and the Public Health Service Hospital in Baltimore) that quality assurance programs in facilities may lead to savings in operational costs. These savings could be used to reduce the costs to patients. Therefore, the purpose of this publication by FDA is to encourage diagnostic radiology facilities to establish their own quality assurance programs with the goals of improving diagnostic image quality and reducing unnecessary patient radiation exposure. The recommendation will also

suggest elements which should be included in such programs. The Notice of Intent for this recommendation elicited considerable interest and endorsement.

(4) Consumer Product Radiation Control

a. Proposed Recommendations 6/30/78, Final Recommendations 12/30/78
FDA - Recommendations on Radioluminous Timepieces

Over the past several decades, radium has been used extensively as the luminizing activator in the paint used on the hands and dials of timepieces available to the consumer public. More recently, tritium and, to some extent, promethium-147 have also come into use for this purpose. To a large extent, these radionuclides have been replacing radium in timepieces. However, recent data indicate that radium—particularly from import sources—is still being used in significant amounts in clocks. Radium constitutes a source of unnecessary radiation exposure that could be significantly reduced or avoided by the use of radionuclides emitting lower energy radiations. The Recommendations to be proposed by FDA will be directed to the State's Radiation Control Program Directors and include the efficacy of the luminescence, the occupational exposure parameters, the dose commitment to the individual and population, alternatives to the use of radium, and radiation warning labeling. Because of the responsibilities of other Federal agencies in this area, involvement in the review and development of these recommendations would also include the Nuclear Regulatory Commission, Consumer Product Safety Commission, U.S. Customs and the Department of Transportation.

b. Interagency Planning Meeting 1/12/78
FDA, CPSC, NRC, Others - Guidelines or Regulatory Standards for Smoke Detectors

FDA, CPSC, and NRC plan to collaborate in the development of guidelines or regulatory standards to protect the public health and safety from hazards associated with consumer products containing radioactive materials such as fire and smoke detectors.

5. Principal Technical Contacts

FDA - Ronald Wylie (Chairperson)	443-3480
Marshall Little	443-3429
Wayne Matthews	443-3480
EPA - Allen Richardson	557-8927
OSHA - David Lee	523-7179
CPSC - Alan Ehrlich	492-6557

6. Recommendation

- A. OSHA should consider initiating steps to revise its regulations concerning radiation protection to make these regulations consistent with new regulations of other Federal agencies (e.g., NRC), with new national guidelines, and with new radiation problems.
- B. The four agencies should assess the present data bases required for regulatory initiatives, especially with regard to the biological effects of low-level radiation (particularly non-ionizing) and should propose studies to fill any identified needs.
- C. Interagency Research and Investigations - Several of the agencies listed in Appendix III are actively engaged in or support research and investigations relating to radiation protection. The radiation-type studies listed below include only those involving interagency collaboration:

Cooperative Studies - Interagency Agreements

<u>Type of Study</u>	<u>Agency & IAG No.</u>	<u>Type Radiation</u>
Biological Effects	EPA-NAS (Support of BEIR) FDA-NBS 224-77-6015 FDA-NIH-NCI 224-77-6007 FDA-ONR 224-77-6003	Ionizing Ionizing Ionizing - nuc. med. Microwave
Use Control		
Prog. Eval.	FDA+5 Agencies & 33 States	Ionizing (ODIS)
Efficacy	FDA-HCFA 224-77-6014	Ionizing (x-ray)
Q.A.	FDA-NIH-NCI 224-77-6001	Ionizing (Mammography)
Personnel Monitoring	FDA+9 Agencies	Ionizing
Fed/State Programs	FDA+2 Agencies (EPA & NRC)	Ionizing & nonionizing
Protection	FDA-USAF 224-75-6002	Light (laser eyewear)
Product Monitoring	FDA-USN 225-77-6001	Microwave (ovens)
Emergency Planning	FDA-ERDA 225-75-6005 FDA-NRC 224-77-6002	Ionizing Ionizing
Education	FDA-HRA 224-77-6008 FDA-NRC 224-77-6004	X-Ray Ionizing (consumer products)
Instrumentation	FDA-NBS 224-77-6009	Ultrasound

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RESPONSIBLE AGENCIES

A number of Federal and State agencies may contribute to the national program for radiation protection as briefly summarized in alphabetical order below. Other details on the activities of these agencies are contained in Section 4.

1. Consumer Product Safety Commission - Establishes product safety standards, where appropriate to reduce the unreasonable risk of injury to consumers from consumer products. It may ban hazardous consumer products. Conducts research on consumer product standards. It has no authority to regulate materials covered by the Atomic Energy Act nor to establish radiation safety standards for electronic products.
2. Department of Energy - Consolidates Federal activities relating to research and development on the various sources of energy, including the advancement of goals to restore, protect, and enhance environmental quality, and to assure public health and safety.
3. Department of Health, Education and Welfare
 - A. Food and Drug Administration - Through the development and enforcement of standards, regulations, and guidelines, protects the health of the nation against impure, ineffective, and unsafe foods, drugs, cosmetics and medical devices, and radiation safety for electronic products.
 - B. National Institute for Occupational Safety and Health - Supports research and establishes criteria to be used for appropriate controls to assure the health and safety in the working environment.
4. Environmental Protection Agency - Advises the President with respect to radiation matters, directly or indirectly affecting health, including guidance for all Federal agencies in the formation of radiation standards and in the establishment and execution of programs of cooperation with states. Abates and controls environmental pollution by integration of research, monitoring, standard-setting, and enforcement of activities for the environment. Coordinates and supports research and antipollution activities by State and local governments and others. Advises the President with respect to radiation matters directly or indirectly affecting health.
5. General Services Administration - The GSA establishes policy and provides for the government an economical and efficient system for the management, procurement and distribution of supplies, utilization and disposal of property—including the disposal through surplus channels by Federal agencies of radiation products and materials.

6. National Bureau of Standards - Provides a national system for physical measurement and services to improve the use of materials and the application of technology.
7. Nuclear Regulatory Commission - Through a licensing and regulatory program, assures that civilian uses of nuclear materials and facilities are conducted in a manner consistent with the public health and safety, environmental quality, national security, and the antitrust laws. The major focus is on the use of nuclear energy to generate electrical power.
8. Department of Labor (Occupational Safety and Health Administration) - Develops, promulgates, and enforces occupational safety and health standards and regulations.
9. Office of Telecommunications Policy - Coordinates the planning and evaluating of the operation of the communication activities of the Executive Branch. This includes the establishment of policies and the setting of standards for Federal communications systems, and overall guidance of Federal research and development efforts.

Sulfur Dioxide (SO₂)

1. Background

A. Health Effects

Sulfur dioxide is a recognized human irritant. Its irritant properties are due to the rapidity with which it forms sulfurous acid on contact with moist membranes.

Sulfur dioxide exerts its toxic influence on humans through acute and possibly chronic effects. Acute symptoms of exposure are eye, mucosal and upper respiratory irritation. Potential chronic effects include nasopharyngitis, reduction of pulmonary function, increased resistance to air flow and promotion of cancer.

Chronic effects may result from repeated bronchoconstriction. While not itself a chronic effect, it is believed that this continued insult actually leads to substantial permanent pulmonary impairment in excess of the normal gradual decrease due to aging.

B. Production/Use

Sulfur dioxide is released as an unwanted by-product of smelting of ores, combustion of some coals and fuel oils, paper manufacturing and petroleum refining. Industrially, sulfur dioxide is an intermediate in the manufacture of sulfuric acid, and is used in refrigeration, bleaching, fumigating and food preserving operations, and as an antioxidant in processing of magnesium.

C. Current Status of SO₂ Regulations

(1) OSHA

- a. The Agency currently enforces a 5 ppm permissible exposure limit for occupational exposure to sulfur dioxide.
- b. In November 1975 a proposed revision to the current permissible exposure limit was published in the Federal Register.
- c. In May of 1977 public hearings were held on the proposal.

(2) EPA

- a. Sulfur oxides (as measured by sulfur dioxide) comprise one of the six air pollutants for which National ambient air standards have been established. The NAAQS is 80 mg/m³ annual average. The 24 hour standard is 365 mg/m³ not to be exceeded more than once per year. Secondary standard (to protect public welfare) is 1300 mg/m³ 3 hour average not to be exceeded more than once a year.

- b. The Sulfur Oxide criteria document is being updated and revision is expected by 1980. No change in permissible exposure limit is anticipated.
- c. Emission limitations have been established for several new source categories, including coal-fired and oil fired power plant boilers, sulfuric acid plants, petroleum refineries, and non-ferrous smelters. Proposed revision is scheduled for early 1978 for power plants.

(3) CPSC

- a. Has no involvement with sulfur dioxide at this time.

(4) FDA

- a. Sulfur dioxide has generally been regarded as safe (GRAS) as a chemical preservative when used in accordance with good manufacturing practice. (It is not used in meats or in food recognized as a source of vitamin B₁.)
- b. The status of SO₂ as a food preservative is being reevaluated. It is anticipated that levels of use will be restricted to those currently in practice.

2. Issues

- A. To what extent are there hypersusceptible individuals in the population and to what extent, if any, should such persons be considered in establishing a standard for exposure to sulfur dioxide?
- B. To what extent, if any, does sulfur dioxide promote cancer?
- C. What are the environmental and inflationary impacts of SO₂ regulations?

3. Statutory Authorities

EPA - Clean Air Act
 FDA - Food, Drug and Cosmetic Act
 OSHA - Section 6(b) of the Occupational Safety and Health Act

4. Principal Actions/Schedules (Tentative)

1971 - OSHA occupational exposure limit
 10/25/71 - EPA National ambient air standard
 10/75 - OSHA proposed revision to standard
 1976 - FASEB evaluation as a food preservative
 5/77 - OSHA hearings on proposed revision
 1978 - OSHA final revision
 1979 - FDA proposal for use as a food preservative
 1978 - EPA revision to emission limitations
 1980 - EPA Criteria Document revision expected

5. Agency Technical Contacts

OSHA - Patricia Waugh	523-7151
EPA - Jack Farmer	8/629-5477 (FTS)
CPSC - Stan Morrow	492-6557
FDA - Scott Andres	472-4750

6. Recommendation

Quarterly meetings to update technical representatives on status of rulemaking, new literature, etc. are recommended.

Vinyl Chloride (VC) - Polyvinyl Chloride (PVC)

1. Background

A. Health Effects

Carcinogenicity studies indicate vinyl chloride is a carcinogen by inhalation and ingestion. It is also a possible mutagen. The chemical is a component of emissions from manufacturing plants. Vinyl chloride, normally a gas, is used to produce a type of plastic called polyvinyl chloride (PVC).

B. Production/Use

Vinyl chloride homopolymers and copolymers are widely used in the packaging industry, building construction, electrical engineering, and automobile products. Food packaging materials, parts for food processing equipment, flexible tubing, and water pipes are among the many food contact applications of this versatile polymer. Properties that make polyvinyl chloride useful for packaging are its clarity, resistance to water and many chemicals, ability to be heat-sealed, and ability to be molded into deep shapes.

In 1975 approximately 300 million pounds of PVC were used in packaging food and 400 million pounds of resin were used in production of water pipe.

C. Current Regulatory Status

(1) EPA

EPA published permanent standards for vinyl chloride emissions from vinyl chloride and polyvinyl chloride but was sued by Environmental Defense Fund because the standards did not provide the ample margin of safety to protect human health required by the Clean Air Act. EPA proposed amendments to the standards on 6-2-77 and extended the comment period until 9-23-77.

(2) FDA

- April 1974, initiated action to ensure that vinyl chloride is not used in any aerosolized food, drug, or cosmetic products.
- FDA requested manufacturers to stop the use of vinyl chloride as a propellant and to recall all outstanding stocks.
- August 1974, FDA issued a regulation banning the use of vinyl chloride as a propellant in aerosol cosmetics and requiring an approved new drug application for marketing.

September 3, 1975, FDA proposed to prohibit rigid and semi-rigid polyvinyl chloride materials for food contact use and to publish regulations establishing safe conditions of use for plasticized films and other prior sanctioned uses of vinyl chloride polymers and copolymers where there was no reasonable expectation of migration. This viewpoint has changed due to several factors: a) new analytical techniques have demonstrated the presence of vinyl chloride monomer in plasticized films and new technology has reduced the residual monomer content of rigid and semi-rigid materials to levels equivalent to those found in plastic films; b) carcinogenicity studies which were in preliminary stages in 1975 have progressed sufficiently to suggest strongly that vinyl chloride is a carcinogen when ingested by laboratory animals; and c) precedent has been set by the Commissioner's decision on use of acrylonitrile polymers and copolymers in bottles (42 FR 48527), September 23, 1977. Four major points were established in the document for acrylonitrile:

- a. Acrylonitrile monomer, which is contained in acrylonitrile polymers is a food additive under section 201(s) of the Federal Food, Drug, and Cosmetic Act.
- b. Acrylonitrile is a probable carcinogen based on available data.
- c. Under the currently accepted diffusion model, any acrylonitrile monomer present in the polymer would be reasonably expected to migrate to food contained in the bottle.
- d. Although migration of the monomer cannot be detected, there is every likelihood that residual monomer is present in the polymer and, hence, will migrate to food.

A final rule banning use of rigid and semirigid polyvinyl chloride should be published during 1978. A new proposal concerning the other uses also should be published in 1978.

(3) OSHA

OSHA Promulgated regulations on October 4, 1974 setting permanent standards for vinyl chloride of 1 ppm averaged over any 8 hour period and a ceiling of 5 ppm over any period less than 15 minutes in work areas. No future action is contemplated at this time other than a literature update.

(4) CPSC

CPSC promulgated a revised regulation classifying self-pressurized household substances containing vinyl chloride as an ingredient or propellant, as banned hazardous substances (March 24, 1978).

2. Issues

- A. Risk/benefit - At the present time, a major difference in regulatory policy exists between FDA, EPA and OSHA. Due to the Delaney Clause,

FDA cannot set a tolerance based on a risk/benefit analysis for food contact use of a known carcinogen. EPA and OSHA both have the leeway to make such a judgment in the setting of their standards, especially where no alternative products exist. FDA rulings against PVC could be used by the Environmental Defense Fund (EDF) or others in suits against EPA or OSHA. It may appear incongruous for FDA to ban PVC because of a level of migration measured in the parts per billion (ppb) range while EPA and OSHA permit air standards measured in the ppm range, but differences in the respective statutory authorities discussed above has created this situation.

- B. Authority over PVC water pipe for potable water - It is not clear whether EPA or FDA has jurisdiction over this use of rigid vinyl chloride polymers. A joint action could be the best way to resolve this problem.
- C. Opportunity for hearings - The statutory authorities for both EPA and OSHA provide opportunities for hearings after regulations are proposed and before promulgation in final form. FDA must hold a hearing only after promulgation of a final regulation. (There is a comment period provided after publication of a proposed regulation.) FDA, however, may hold a hearing before promulgation of a final regulation.

3. Statutory Authority

EPA - Section 112 of the Clean Air Act gives authority to set standards, which provide an ample margin of safety to protect human health from hazardous air pollutants.

FDA - Section 409, of the Federal Food, Drug, and Cosmetic Act gives authority to issue regulations prescribing safe conditions of use for food additives. Section 409(c)(3), the Delaney Clause, prohibits the addition to food of any additive which is found to induce cancer when ingested by man or animal.

OSHA - Sections 6 and 8 of the Occupational Safety and Health Act of 1970 gives authority to prescribe standards for any substance to protect humans from suffering material impairment of health during their working time while in private employment.

CPSC - Section 2(q)(1)(B) of the Federal Hazardous Substances Act defines banned hazardous substances and is authority for the current bans.

4. Principal Actions/Schedules (Tentative)

3/24/78- CPSC ban on use of Vinyl Chloride as aerosol propellant.

Spring - EPA promulgation of amended final rule for vinyl
78 chloride emissions from manufacturing plants.

Summer - FDA promulgation of tentative final rule based
78 on the proposal of 9-3-75 concerning rigid and semi-rigid polyvinyl chloride materials for food contact use.

12/78 - FDA proposal concerning other uses of PVC in contact with food.

Open - OSHA updated Literature Search.

5. Technical Contacts

EPA - Susan Wyatt	8/629-5421 (FTS)
FDA - Gerad L. McCowin	472-5740
OSHA - Eugene Regad	523-7176
CPSC - Francine Shacter	492-6557

6. Recommendations

- A. Jurisdiction over PVC water pipe - Resolve jurisdiction over PVC water pipe or agree upon joint action by EPA, FDA and CPSC to establish safe conditions of use.
- B. Sharing of information - This would be the primary basis of inter-agency cooperation. Each Agency appears to have access to data that other agencies do not have. Steps were taken during the workgroup meeting of November 29, 1977 to share information among the agencies. New toxicological information will soon be available on vinyl chloride. Each of the agencies concerned have almost completed their current regulatory actions on this substance, but will inform the other of any new regulatory actions when they are contemplated.
- C. Regulations - Drafts of final regulations should be circulated to other agencies prior to publication.
- D. Environmental and Economic Impact Assessment Statements - Duplication of effort, time and expense may be incurred because each Agency prepares its own environmental and economic assessments and statements. FDA was not required to file an EIS for VC and its proposed regulation due to the small percentages of total PVC production which were affected by its action. It was suggested during the meeting that a joint effort in preparing these assessments could serve to reduce possible duplication.
- E. Consideration of modification of regulatory standards to develop a consistent standard to the extent that is possible within the context of varying statutory authority.

Waste Utilization or Disposal on Food Chain Land

1. Background

A. Purpose

This plan spells out the interagency coordination in the review of policy and rulemaking activities concerning disposal or utilization of waste (e.g., sludge, wastewater, effluent, ground refuse, waste derived agricultural products, etc.) on land used for the production of food or feed. Currently, the FDA and EPA are the primary participants.

The plan is a direct result of the initiative taken by the heads of four agencies in forming the IRLG. CPSC and OSHA have decided not to participate in the development or implementation of this particular work plan as these agencies have few functions which presently are significantly related to the issue of concern. However, either CPSC or OSHA may express a future desire to formally or informally review particular policy or rulemaking items. The exercising of this option is at the discretion of either of these agencies, and EPA and FDA should assume responsibility for alerting them as to rule and policy making which may be within their scope of interest.

Prior to this interagency agreement, an informal practice existed between EPA, FDA, and the U.S. Department of Agriculture of circulating rulemaking and major policy documents for comment. The formalization of this process for FDA and EPA enhances this already existing coordination. Although USDA is not a party to the IRLG, it continues to be an essential reviewer of such documents.

It is recognized that due to the nature of the individual responsibilities within EPA and FDA concerning waste disposed or utilized on food chain land, there may well be an unequal number of documents circulated by the respective agencies. However, the intent of this work plan is not to attempt to equalize the involvement of each agency but to provide for the coordination of several Federal perspectives.

The primary concern of FDA on this issue is not about the type of contaminant bearing waste which is disposed or utilized but about the potential for contamination of food or feed. In other words, FDA interests lie in protecting the human and animal diet from hazardous (from the FDA point of view) contamination regardless of source.

Historically, EPA has dealt with the disposal or utilization of waste in the food chain on a waste specific basis and in some areas (e.g., effluents) this continues to be the case. However, a large portion of wastes so utilized are solid wastes (as defined by RCRA), and for these, the protection of food and feed will be dealt with in an overall manner (RCRA Subtitle D, Solid Waste Disposal Facility Regulations). The concern within these solid waste regulations will be for the contamination of land and food or feed regardless of the particular solid waste source of contaminants.

Therefore, in order to best meet the needs of both agencies and to most fully utilize the interagency coordinative agreement, the work plan applies to the disposal or utilization of all waste on land used for the production of food chain crops including wastewater, sludges and effluents.

The overall objectives of this coordinated program are:

- (1) To improve public health protection from toxic or hazardous contaminants which may enter the human food chain as a result of waste disposal or utilization.
- (2) To provide coordinated and consistent Federal policy, regulations, and guidelines, share information, minimize duplication of effort, and in general, to work together in a closely cooperative manner.

B. Health Effects

The health and environmental problems associated with wastes which are disposed or utilized on food chain land are directly related to the quality of the waste, characteristics of the disposal site, application rate of the waste to the soil, and several other major management variables.

Because of the heavy metal, toxic organic, pesticide, and micro-biological content of many wastes applied to food chain land, improperly controlled disposal or utilization poses a risk to public health and the environment (through excessive crop uptake, direct ingestion by humans and animals, surface runoff, etc.). For example, application of municipal wastewater treatment plant sludges to food chain crops has been shown, with few exceptions, to increase the cadmium concentrations in these crops. FDA has indicated that significant cadmium increases in human foods, whatever their source, are undesirable.

It is recognized that interagency efforts concerning waste utilization or disposal on food chain land must include close contact with other IRLG regulatory development work groups as, in many instances, these chemicals are contaminants of wastes so disposed or utilized. Therefore, for optimal protection of public health and the environment, activities within the scope of this work plan must remain continually receptive to the conclusions of other IRLG work groups.

C. Production/Use

Wastes disposed or utilized on food chain lands include municipal wastewaters, effluents and sludges cannery wastes, pulp and paper mill wastes, petroleum company wastes, feedlot wastes, some limestone scrubber wastes from coal-fired utilities, and other wastes.

Agricultural utilization of sludges from municipal wastewater treatment plants is expected to significantly increase over the next decade as a result of greater sludge generation rates, cessation of ocean disposal, and an increased emphasis upon beneficial utilization of these wastes. Currently, about 20% of the nation's municipal sludge, or about one million dry tons per year, is applied to land for the production of food and feed.

It is in this area of municipal sludge disposal and utilization that the most intense research has occurred and, consequently, the most complete data is available.

D. Current Status of Regulations

(1) Current Programs:

EPA currently has few rules in effect regulating the disposal or utilization of waste on food chain land. However, solid waste disposal regulations which are being developed for under RCRA, Subtitles C and D, will provide Controls for the disposal of solid waste. Regulatory control over the utilization or disposal of wastes not covered by the RCRA definition of solid waste, such as municipal wastewater and effluent used in the production of food or feed, may also be needed.

Under the CWA the granting of funds for the construction of publicly owned sewage treatment works provides EPA with a partial mechanism for the control of sludge wastewater and effluent disposal or utilization on land. This control can be accomplished by the approval of only those grant applications which provide an acceptable utilization or disposal method. A non-regulatory technical bulletin on municipal sludge management practices has been issued as guidance to the EPA Regional Administrators in evaluating sludge management plans submitted for funding under the construction grants program.

Pursuant to Section 402 of the CWA, EPA requires the permitting of point source discharges to surface waters. The standards to be met for effluent discharge from municipal wastewater treatment plants to surface waters help to determine the quality of sludge which must be disposed or utilized.

Also under the CWA (Section 405), EPA is developing regulations for the utilization or disposal of sludge from municipal wastewater treatment plants. Controls will be established for landspreading and giveaway or sale of sludge.

FDA is conducting studies of certain contaminants in various foods and may from time to time establish maximum contamination limits (under provisions of the Federal Food, Drug, and Cosmetic Act) in various foods for the purpose of protecting the health and well-being of the human and animal diet. Wastes such as sewage sludge, wastewater, or effluent contain certain contaminants which are of concern to FDA, and research has shown that improper utilization or disposal of these wastes can endanger the diet.

(2) Future Implementation:

a. Rulemaking Activities

The following are examples of rulemaking activities which should receive maximum interagency attention throughout the developmental

process. It is recommended that both the proposed and final rulemaking packages which are being sent for review at the Assistant Administrator level (EPA) or at the Associate Commissioner level (FDA) contain the formal comments (if any have been made) of the reviewing agency. These may either be attached to or addressed in the transmittal letter accompanying the rulemaking package. Formal review comments should be received from the reviewing agency within three weeks of solicitation. The program office will transmit the document for formal review on dates which it determines to be most appropriate.

If and when revision of the final documents occurs interagency formal review and comment must again be requested:

- (1) FDA Food Contaminant Levels - Maximum allowable levels may at some time be set for certain contaminants in food and feed.
- (2) Wastewater Treatment Regulations - Under CWA, regulations of concern are those which may significantly affect the procedures for food chain utilization (or disposal) or may significantly affect the quality of municipal and appropriate industrial sludge or effluent to be utilized (or disposed). (Regulations and standards for construction grants (Title II), NPDES implementation (Section 402), and industrial pretreatment (Title III) are of particular interagency interest).
- (3) Toxic Substance Control Regulations - Under the Toxic Substances Control Act. Regulations may specify disposal requirements for certain toxic substances.
- (4) Solid Waste Disposal Facility Regulations - Under RCRA, Subtitle D. These will include a section specifically addressing food chain utilization of solid waste.
- (5) Hazardous Waste Regulations - Under Subtitle C of RCRA. Criteria for the defining of hazardous waste and requirements for hazardous waste disposal.
- (6) Landspreading Guidelines - Under RCRA, Section 1008. Suggested guidelines for landspreading of solid wastes. Greatest care and attention will be focused on food chain land application.
- (7) Municipal Sludge Utilization and Disposal Regulations - Under CWA, Section 405. Of particular interest are landspreading and giveaway or sale requirements.

b. Major Policy Activities

On the following items, active interagency participation should be solicited. However, this work plan intentionally does not specify the level of participation as this is a matter which should be determined by that office. This list includes only those documents which are currently foreseen and should be expanded to include any outputs which the program offices determine to be directly related to the "Key Issues" listed in this work plan.

EPA Sludge Strategies - EPA policy concerning the disposal or utilization of municipal or industrial sludges.

Home Use Bulletin - Suggested guidance for the use of sewage sludge and sludge products around the home. (CPSC review suggested.)

Wastewater Treatment Activities - Technical bulletins and other guidance documents for the implementation of the construction grants program.

2. Issues

The following Key Issues are those which are common concerns for both EPA and FDA (as well as USDA) and which should receive interagency review when discussed in rule or major policy making documents concerning food chain utilization or disposal of wastes. These issues are vital to the interests which both agencies have in establishing this cooperative program.

- A. Levels of contaminants in: waste, crops, and foods.
- D. Application rates of contaminants.
- E. Microbiological concerns.
- F. Types of crops grown.
- G. Home vegetable garden use of wastes (CPSC review suggested).

3. Statutory Authorities

- FDA - Federal Food, Drug and Cosmetic Act - Food contaminant levels
- EPA - Clean Water Act, Title II - grants for the construction of wastewater treatment works
 - Clean Water Act, Title III - industrial pretreatment regulations
 - Clean Water Act, Section 402 - National Pollutant Discharge Elimination System
 - Clean Water Act, Section 405 - Municipal sludge utilization and disposal regulations
 - Toxic Substances Control Act - Disposal of specific toxic substances
 - Solid Waste Disposal Act, Subtitle D - Disposal facility regulations
 - Solid Waste Disposal Act, Subtitle C - Hazardous waste disposal facility regulations

4. Proposed Actions/Schedules (Tentative)

- Spring 79 - Municipal Sludge Utilization and Disposal Regulations
- Fall 79 - Home Use Bulletin
- Spring 70 - Municipal Sludge Strategy
- Early 79 - Solid Waste Disposal Facility Regulations
- Early 79 - Landspreading Guidelines
- Late 78 - Hazardous Waste Regulations
- Open - Wastewater Treatment Regulations
- Open - FDA Food Contaminant Levels

5. Agency Technical Contacts

EPA - Bob Tonetti	755-9120
FDA - George Braude	245-1152

6. Recommendations

- A. This work plan is a means for one agency to provide direct input to the rule and policy making processes within the companion agency. The level of review and comment (formal or informal) is flexible, reflecting to the interests and priorities of the reviewing agency. However, on rulemaking activities, the program office must request formal comments, regardless of the level (formal or informal) which may later be selected by the reviewing office (for comment on the particular document). Through review and amendment, beginning with preliminary drafts of the subject documents, a consistent Federal program can evolve.

The work plan provides for:

- FDA review and comment (formal or informal) at key stages of development on EPA rule and major policy making documents which concern or may result in the disposal or utilization of any wastes on land used for the production of food or feed.
- EPA review and comment (formal or informal) at key stages of development on FDA rule and major policy making documents which may affect the disposal or utilization of waste in the production of food or feed.

The need for interagency review can be assessed by referring to the "Key Issues" of common concern listed in paragraph 2. If a document is a matter of agency policy significantly concerning any of those Issues, then it should be transmitted for review. In the section on Future Implementation, interagency comments on rule or policy making items are differentiated as to (1) the extent that formal or informal comments are to be solicited and (2) what level(s) of consideration the comments should receive.

State and local governments and the general public are greatly encouraged to participate in the development of all policy, regulations, and guidelines concerning the disposal or utilization of wastes in the production of food or feed. The States are encouraged to develop their own management programs which conform to Federal regulations and guidelines for waste so utilized. It is the localities' primary responsibility to insure that food chain waste utilization or disposal proceeds carefully on an operational basis and in accordance with Federal and State standards.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PLANNING AND MANAGEMENT

Input Department
National Technical Information Service
5285 Port Royal Road
Springfield, Va. 22161

To whom it may concern:

*ck.
returned*

Please find enclosed one (1) copy of the Interagency Regulatory Liaison Group's publication on hazardous substances. I would like you to make this document available for distribution and have enclosed a check in the amount of \$10.00 which I understand is the registration fee.

Should you have any questions, please call me at 755-9010.

Very truly yours,

Glenda Sullivan

Chris Kirtz
Standards and Regulations
Evaluation Division
(PM-223)

*1-12-79
Mr. Kirtz today
told me he had
his back.*

(Enclosure)

Case File